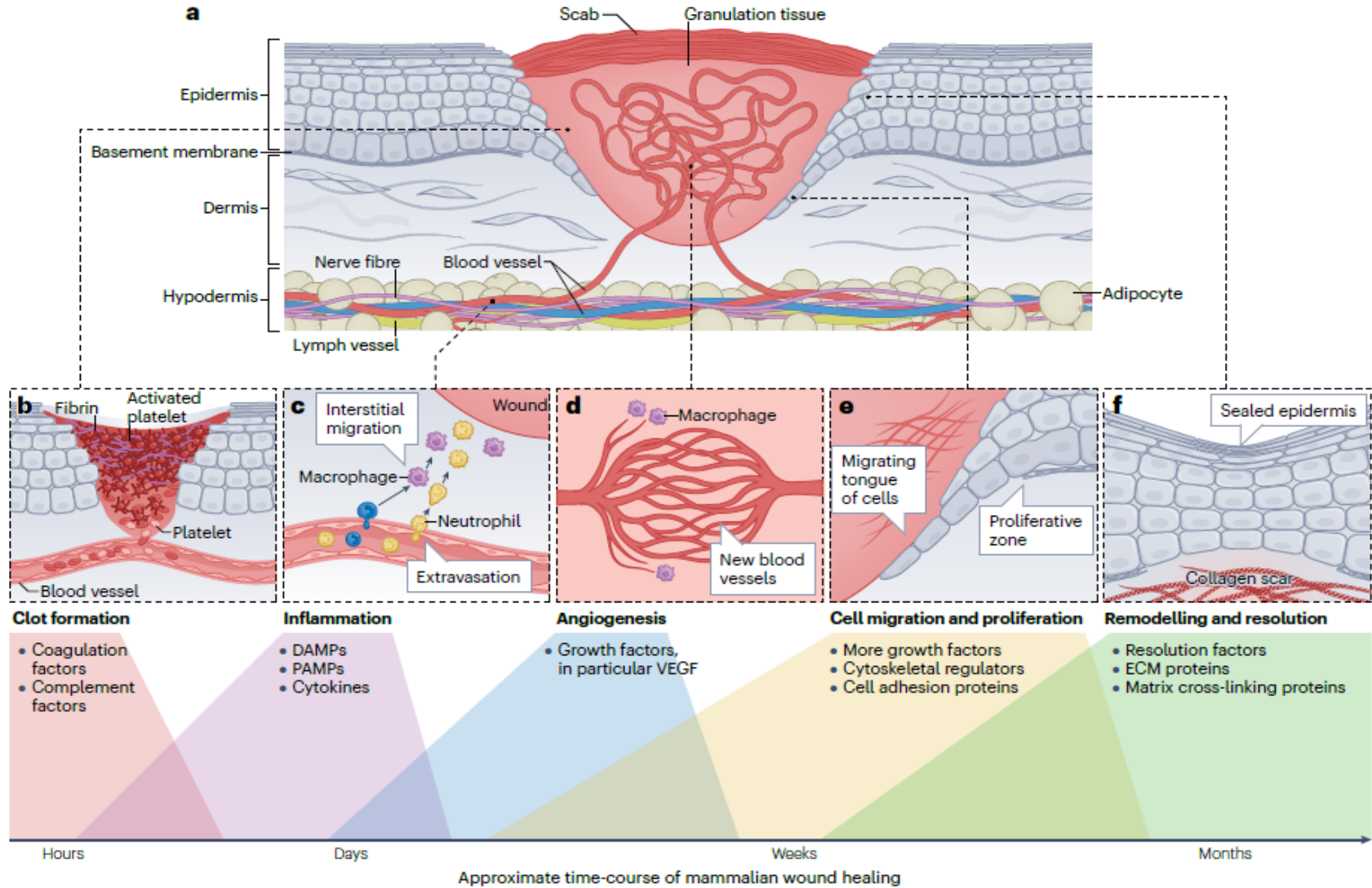


# Next-gen skin research: microfluidic organ-on-chip systems as a key to more realistic models

**PD Dr. Cornelia Wiegand**  
Dermatologisches Forschungslabor  
Klinik für Hautkrankheiten  
Universitätsklinikum Jena

# Cellular interactions during wound healing



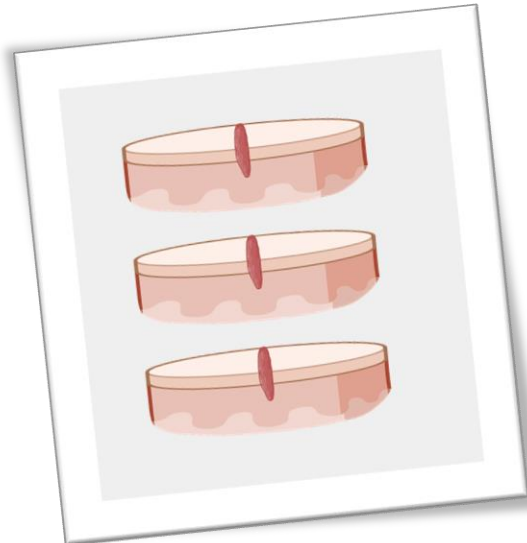
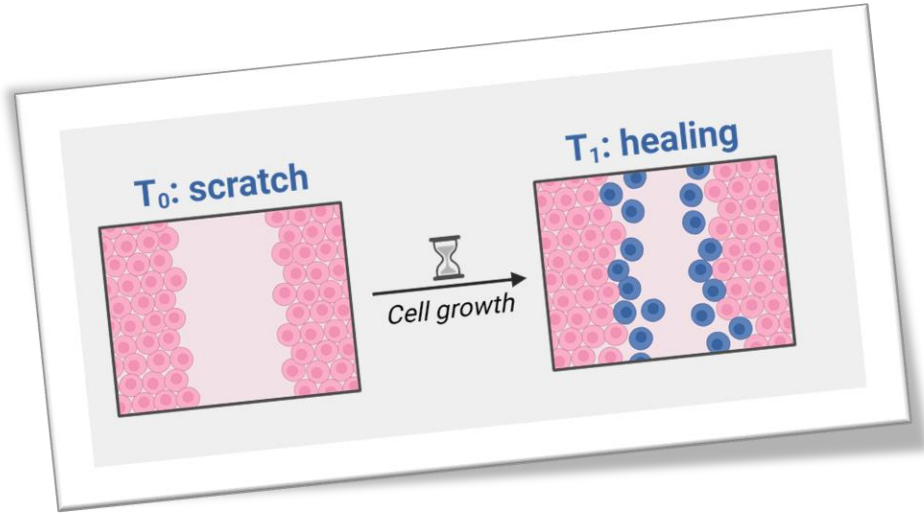
DAMPs, damage-associated molecular patterns  
PAMPs, pathogen-associated molecular patterns

ECM, extracellular matrix  
VEGF, vascular endothelial growth factor

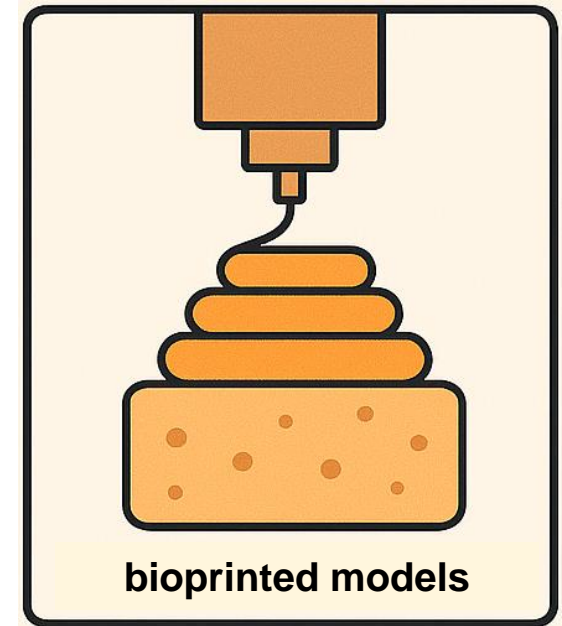
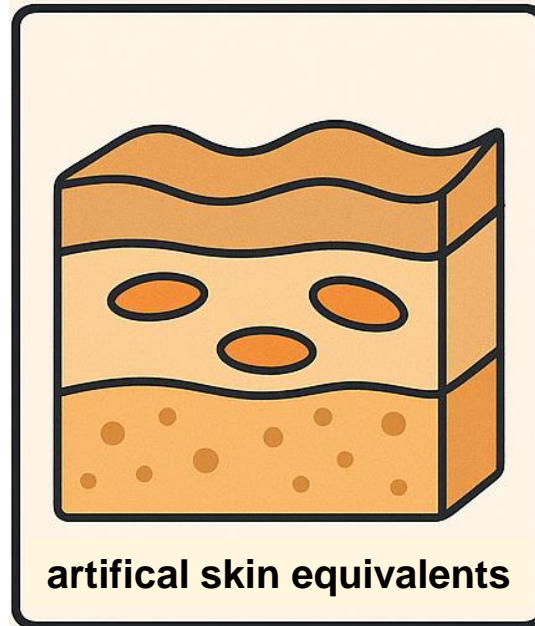
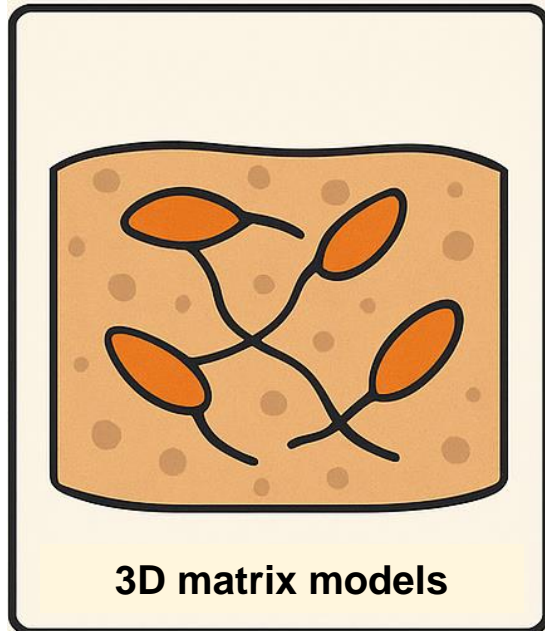
[Pena & Martin Nat Rev Mol Cell Biol 2024]

introduction model examples skin-on-chip summary & outlook

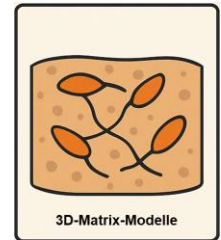
# Common wound models



# 3D skin / wound models - categories



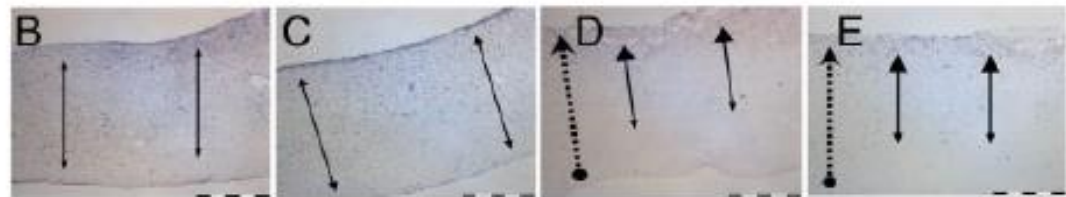
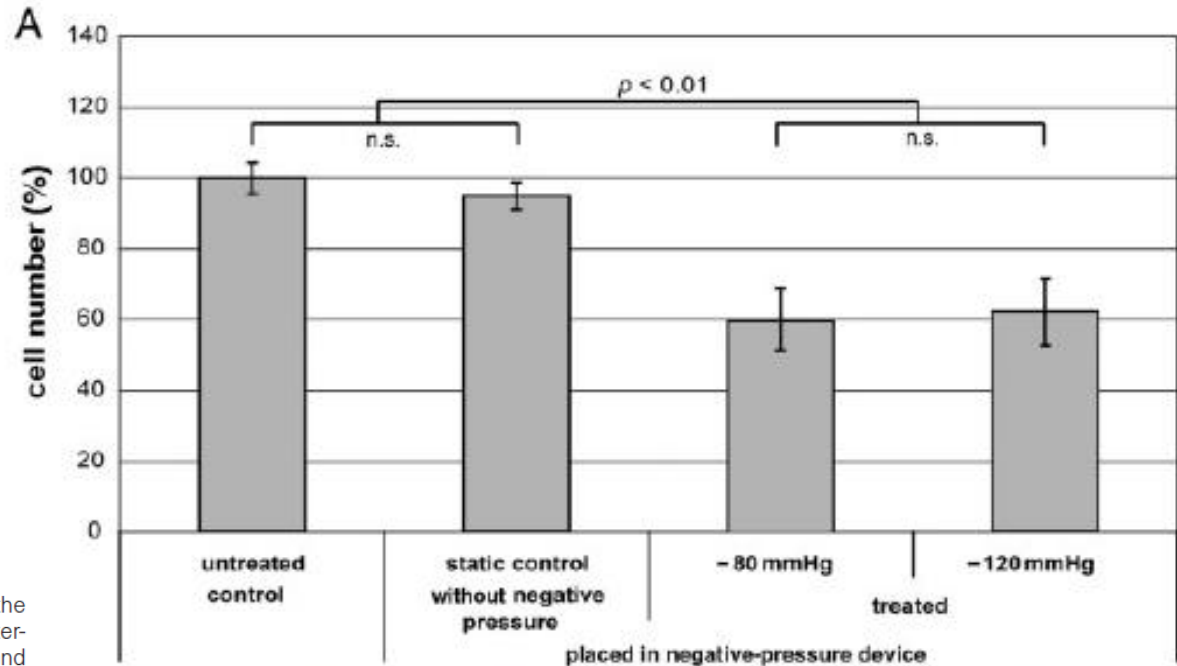
# Matrix models



## Application of a drainage film reduces fibroblast ingrowth into large-pored polyurethane foam during negative-pressure wound therapy in an in vitro model

Cornelia Wiegand, PhD<sup>1</sup>; Steffen Springer, MSc<sup>1</sup>; Martin Abel PhD<sup>3</sup>; Falko Wesarg MSc<sup>2</sup>; Peter Ruth PhD<sup>3</sup>; Uta-Christina Hipler, PhD<sup>1</sup>

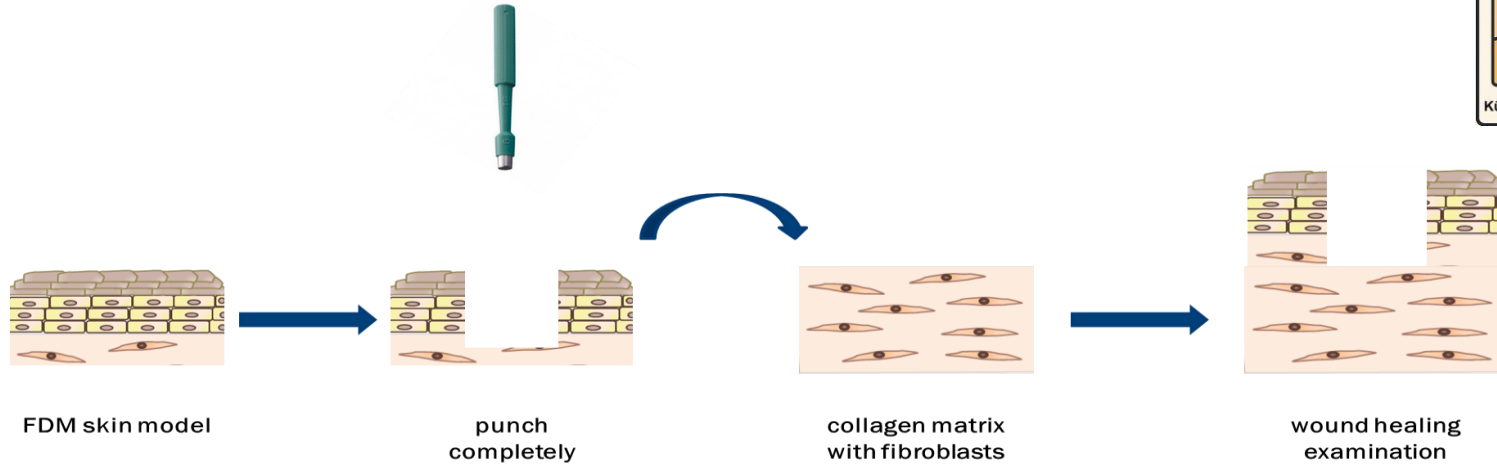
- 1. Department of Dermatology, University Medical Center Jena, and
- 2. Institute of Materials Science and Technology, Friedrich Schiller University J
- 3. Lohmann & Rauscher GmbH & Co. KG, Regensburg, Germany



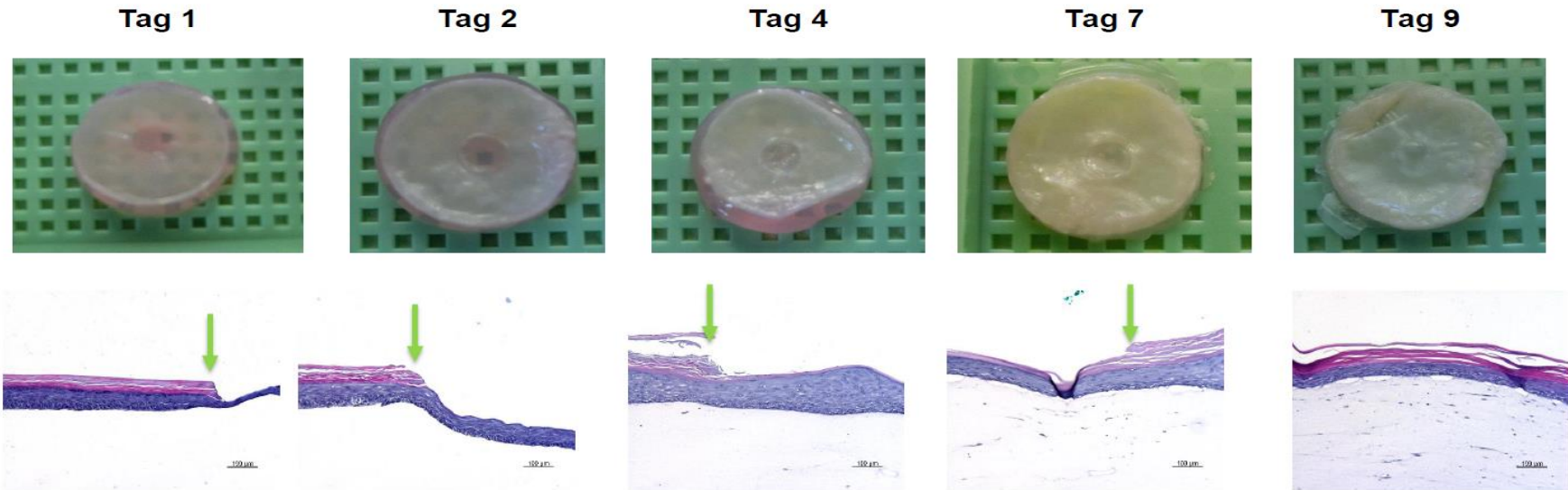
**Figure 1.** (A) Determination of the number of living cells in the 3D human dermal fibroblast (3D hDF) cultures by CellTiter-Blue viability assay after exposure to -80 mmHg and -120 mmHg for 48 hours. Data presented as mean ± SD. (B) Cross sections of 14-day-old fibroblast cultures stained with hematoxylin and eosin. A fibroblast culture designated as static control (C) compared with fibroblast cultures after 48 hours of negative-pressure wound therapy at -80 mmHg (D) and -120 mmHg (E). The dotted arrows specify the direction of the applied vacuum. Double arrows indicate the preferred direction for cell migration. Scale bar = 500 µm.

introduction model examples skin-on-chip summary & outlook

# Artificial skin equivalents



wound healing progression over time – mechanical wound



[Fink et al. presented at the ADF conference 2022]

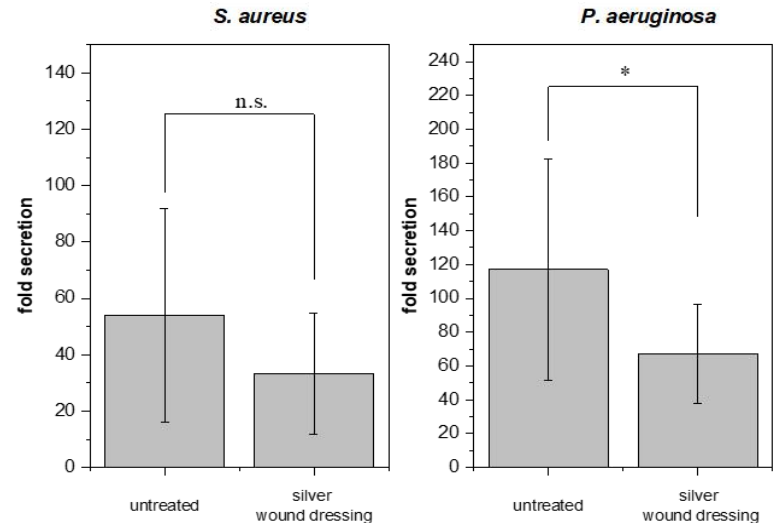
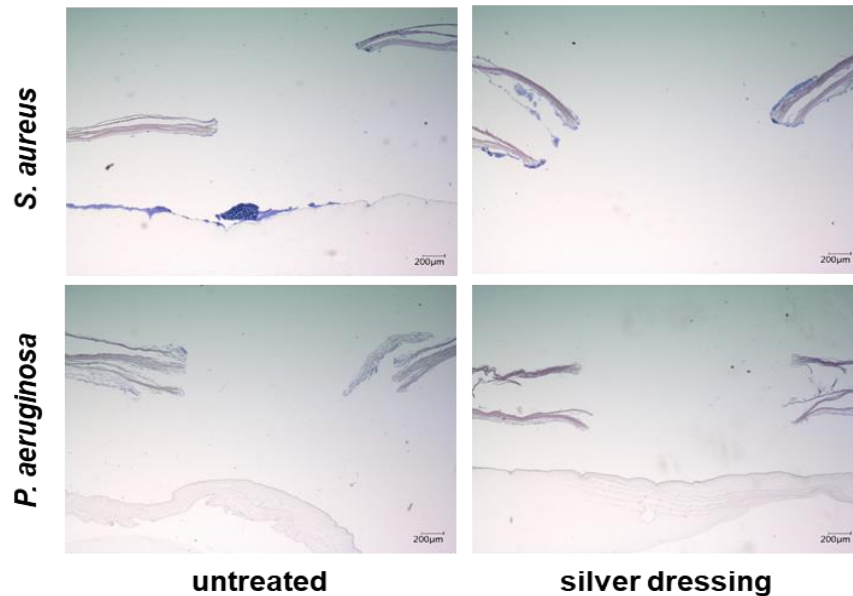
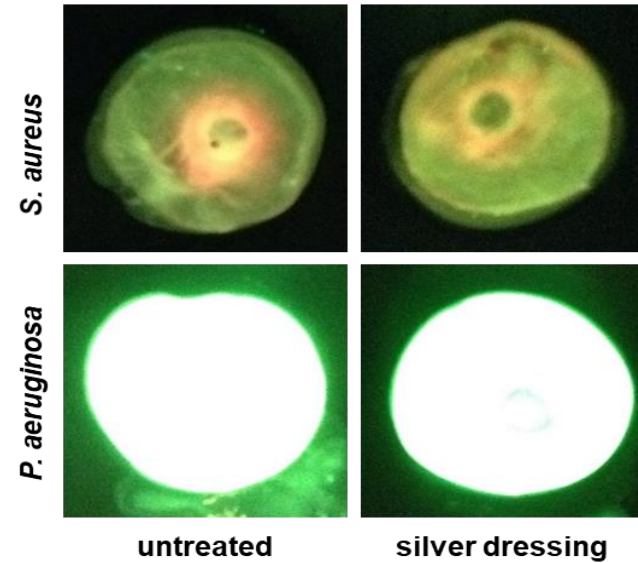
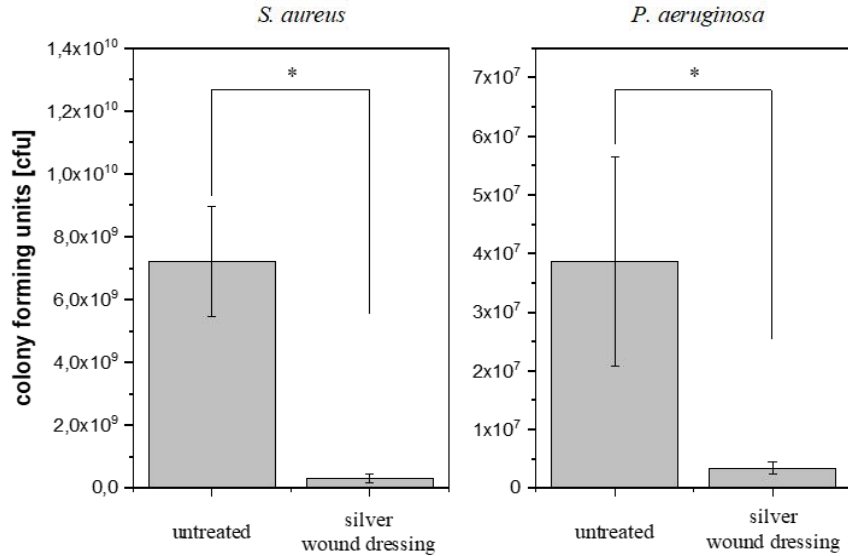
summary & outlook  
skin-on-chip  
model examples  
introduction

# Antimicrobial treatment of infected wound models

skin-on-chip summary & outlook

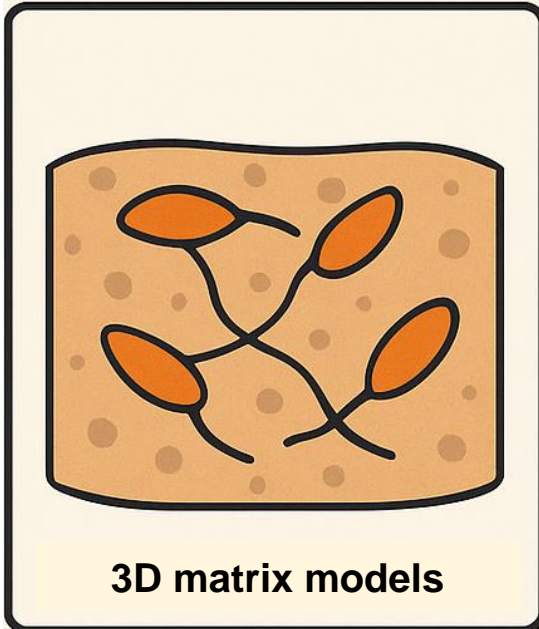
model examples

introduction



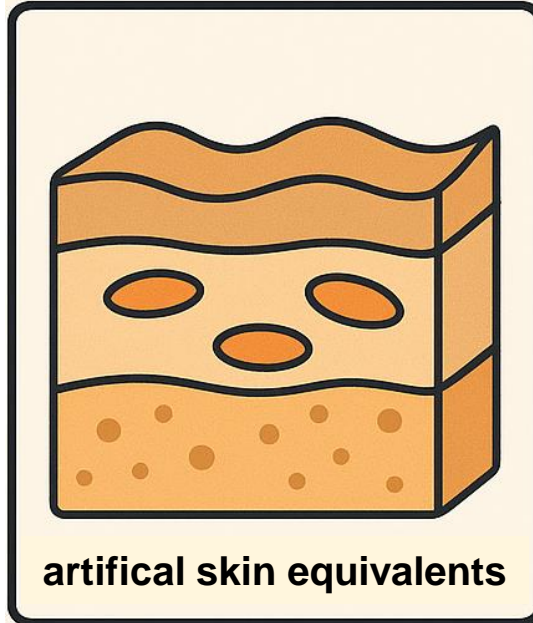
# 3D skin / wound models - categories

May lack complete skin structure and cellular diversity



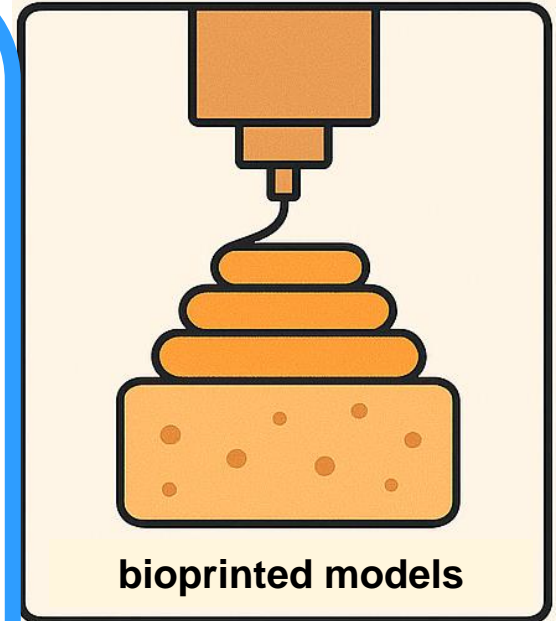
Replication of the extracellular matrix, enable the investigation of cell-matrix interactions

More complex to manufacture, possibly lower reproducibility



High biological authenticity, multiple cell types, layered structure

Technical challenges, specialized equipment required



Precise control of structure, Potential for high complexity

# Increasing complexity of 3D skin models

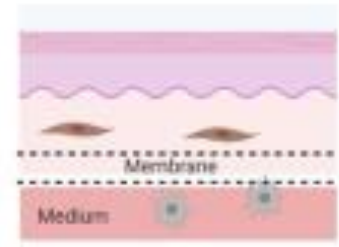
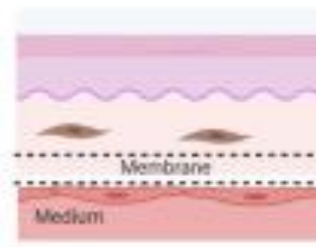
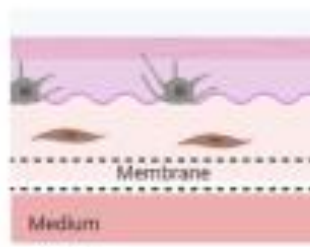
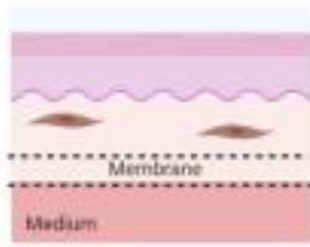
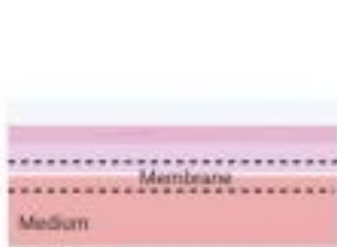
Reconstructed Human Epidermis (RHE)  
 ✓ Keratinocytes

Human Skin Equivalent (HSE)  
 ✓ Keratinocytes  
 ✓ Fibroblasts

Pigmented HSE  
 ✓ Keratinocytes  
 ✓ Fibroblasts  
 ✓ Melanocytes

Vascularized HSE  
 ✓ Keratinocytes  
 ✓ Fibroblasts  
 ✓ Endothelial cells

Immune competent HSE  
 ✓ Keratinocytes  
 ✓ Fibroblasts  
 ✓ LC// Dermal DC



Complexity

Application  
 ✓ Skin corrosion and irritation  
 ✓ Sensitisation potential

Application  
 ✓ Permeation  
 ✓ Skin corrosion and irritation  
 ✓ Skin metabolism  
 ✓ Wound healing

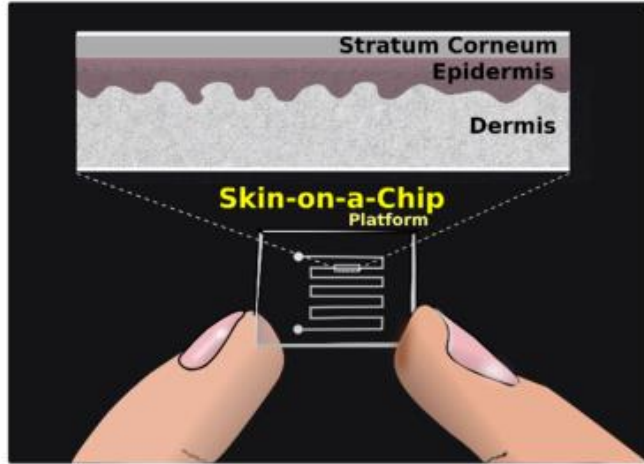
Application  
 ✓ Investigate photosensitive effects  
 ✓ Vitiligo pathogenesis

Application  
 ✓ Permeation  
 ✓ Skin corrosion and irritation  
 ✓ Neutrophil migration

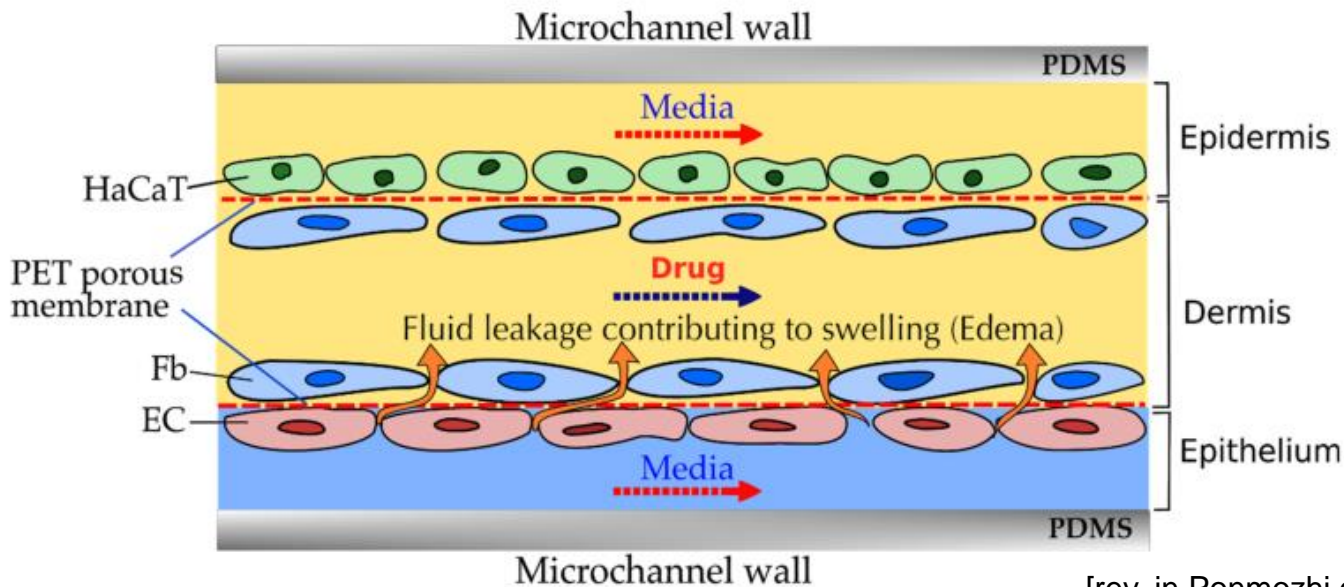
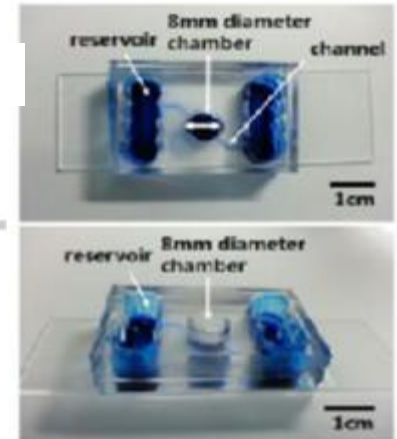
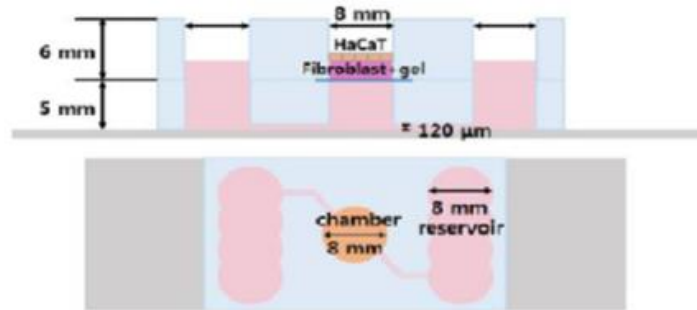
Application  
 ✓ Permeation  
 ✓ Skin corrosion and irritation  
 ✓ Skin sensitization  
 ✓ Skin inflammation  
 ✓ Immune modulation

summary & outlook  
skin-on-chip  
model examples  
introduction

# Skin-on-Chip systems



Sketch of a microfluidic skin-on-a-chip platform.



summary & outlook  
skin-on-chip  
model examples  
introduction

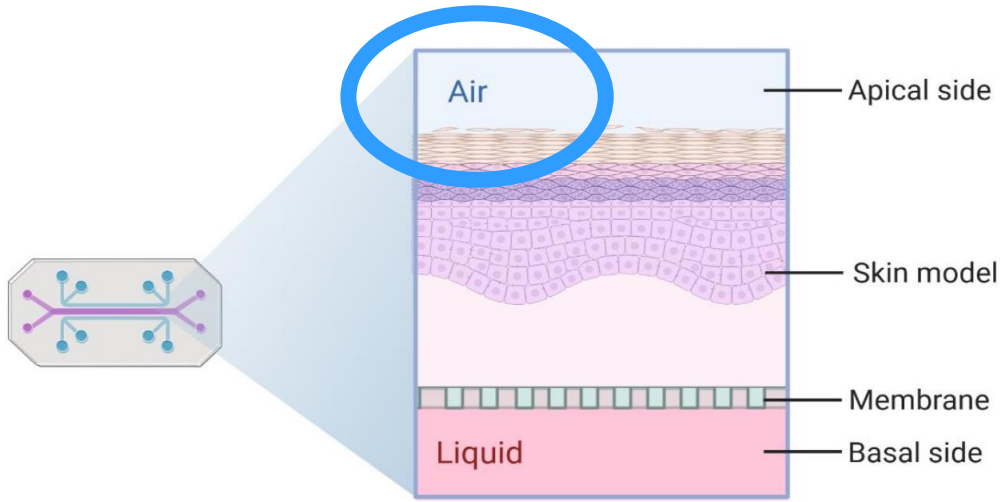
# “Real” Skin-on-Chip systems

summary & outlook

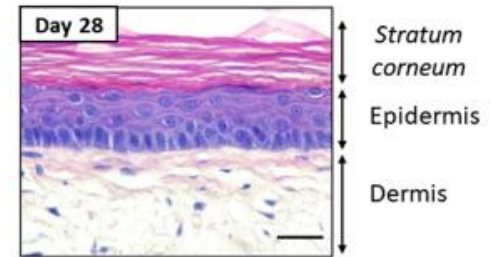
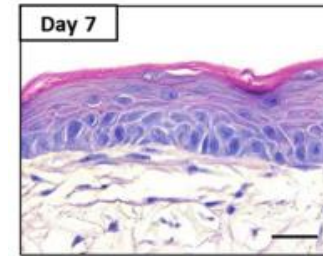
skin-on-chip

model examples

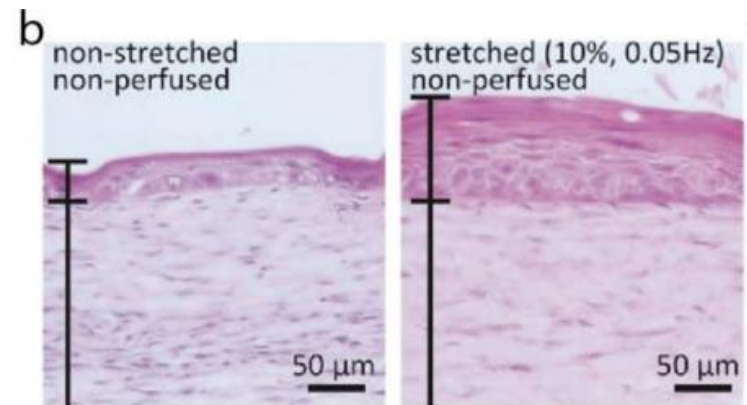
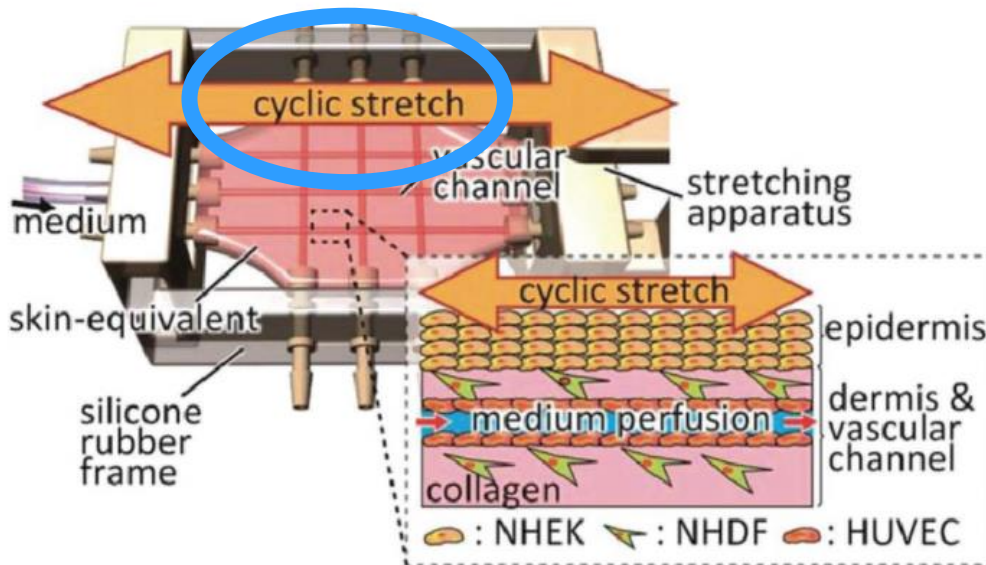
introduction



[Zoio & Oliva. Pharmceutics 2022]

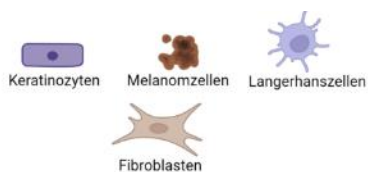
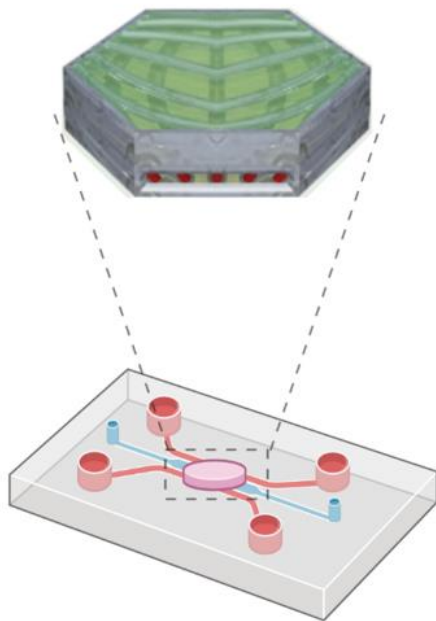


[Risueno et al. APL Bioeng 2021]

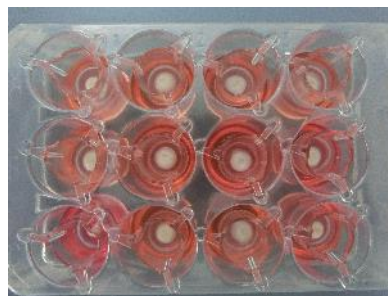


[Zoio & Oliva. Pharmceutics 2022]

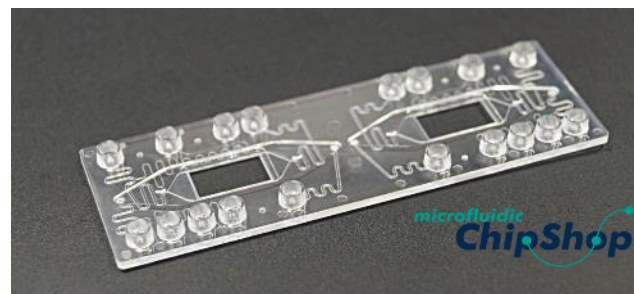
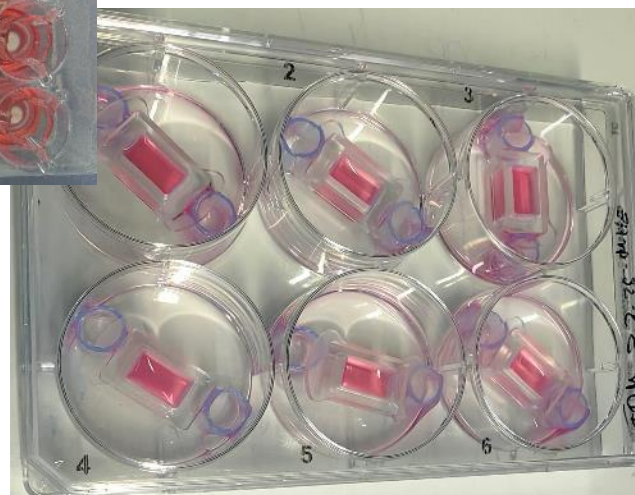
# 3D-ToCA: 3D malignant melanoma skin model



Immunkompetente  
3D-MM-Modelle



transfer  
from round  
to **square**  
inserts to fit  
the chip



summary & outlook

skin-on-chip

model examples

introduction



Kofinanziert von der  
Europäischen Union



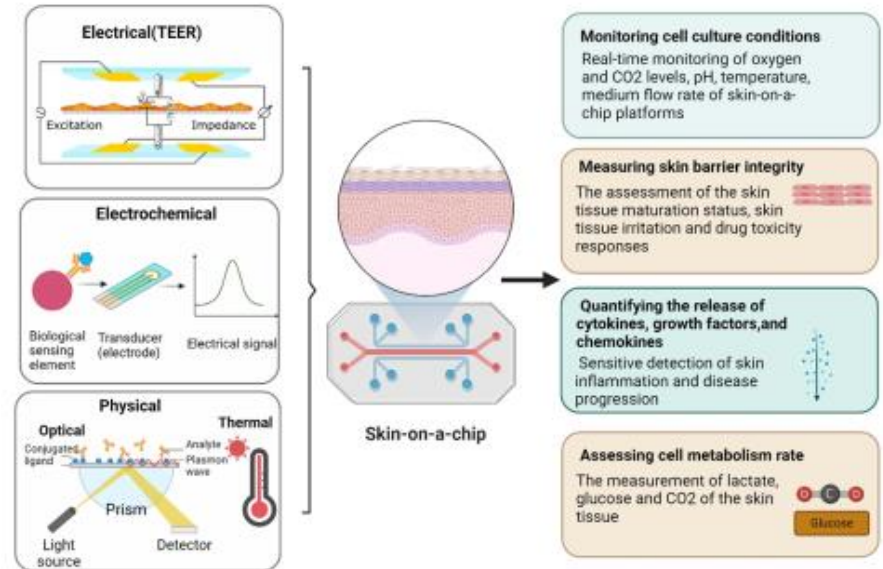
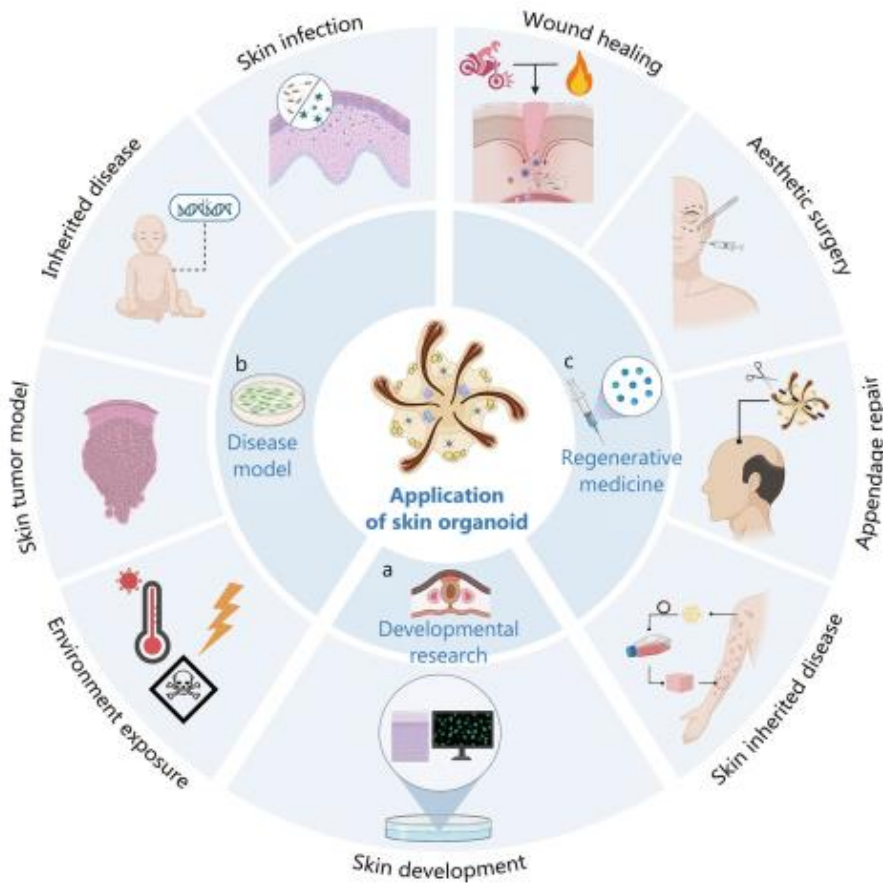
Ministerium  
für Wirtschaft, Wissenschaft  
und Digitale Gesellschaft



# Summary

# &

# Outlook



[Hong et al. Military Medical Research 2023]

[Ismayilzada et al Biofabrication 2024]

introduction model examples skin-on-chip summary & outlook