The use of 3D skin equivalents mimicking skin cancers: unraveling the heterogeneity of cancer-associated fibroblasts and validating therapeutic efficacy

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Appendices

List of abbreviations

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List of abbreviations:

Abbreviation	Full Term
3D	Three-dimensional
Ab	Antibody
ACAN	Aggrecan
AEC	3-amino-9-ethylcarbazole
AFI	Average Fluorescence Intensity
ANOVA	Analysis of Variation
apCAF	Antigen-presenting Cancer-Associated Fibroblast
ASPN	Asporin
BCC	Basal Cell Carcinoma
BM	Basement Membrane
BLIMP	B Lymphocyte–Induced Maturation Protein
CAF	Cancer-Associated Fibroblast
CAV1	Caveolin-1
CASP	Caspase
C-C3	Cleaved Caspase 3
CCL	C-C Motif Chemokine Ligand
CCRL1	C-C Motif Chemokine Receptor-Like 1
CD	Cluster of Differentiation
CDH2	Cadherin-2
CDKN2A	Cyclin-Dependent Kinase Inhibitor 2A
CLEC3B	C-Type Lectin Domain Family 3 Member B
CLU	Clusterin
CM	Conditioned Media
CNN1	Calponin-1
COL	Collagen
COX	Cyclooxygenase
CRP	Carboplatin
CSPG4	Chondroitin Sulfate Proteoglycan 4
CTGF	Connective Tissue Growth Factor
CTLA4	Cytotoxic T-Lymphocyte–Associated Protein 4
CXCL	C-X-C Motif Chemokine Ligand
CXCR	C-X-C Motif Chemokine Receptor

DAPI	4′,6-diamidino-2-phenylindole
DCFDA	Dichlorodihydrofluorescein D iacetate
DCN	Decorin
DED	De-Epidermized Dermis
DEG	Differentially Expressed Gene
DEJ	Dermal-Epidermal Junction
DiD	1,1’-dioctadecyl-3,3,3‘,3’-tetramethylindodicarbocyanine
DLK1	Delta-Like Non-Canonical Notch Ligand 1
DMEM	Dulbecco’s Modified Eagle’s Medium
DMF	Dimethylformamide
DOX	Doxorubicin
ECM	Extracellular Matrix
EMT	Epithelial-Mesenchymal Transition
ENG	Endoglin
FACS	Fluorescence-Activated Cell Sorting
FAK	Focal Adhesion Kinase
FAP	Fibroblast Activation Protein
FASL	Fas Ligand
FBS	Fetal Bovine Serum
FSC	Forward Scatter
FSP1	Fibroblast-Specific Protein-1
FTM	Full-Thickness Model
FZD7	Frizzled Class Receptor 7
GEMM	Genetically Engineered Mouse Model
GM-CSF	Granulocyte-Macrophage Colony-Stimulating Factor
GPR77	G Protein-Coupled Receptor 77
HA	Hyaluronic Acid
HDAC	Histone Deacetylase Inhibitor
HE	Hematoxylin and Eosin
hBD	Human Beta-Defensin
HES1	HES Family bHLH Transcription Factor 1
HGF	Hepatocyte Growth Factor
HLA	Human Leukocyte Antigen
HNSCC	Head and Neck Squamous Cell Carcinoma

HOPX	HOP Homeobox
HPRT	Hypoxanthine-Guanine Phosphoribosyltransferase
HSE	Human Skin Equivalent
HV	Healthy Vulvar
HVF	Healthy Vulvar Fibroblast
HVKC	Healthy Vulvar Epidermal Keratinocyte
IC50	Half Maximal Inhibitory Concentration
ICD	Immunogenic Cell Death
IDO	Indoleamine 2,3-Dioxygenase
IF	Immunofluorescence
IGFBP7	Insulin-Like Growth Factor Binding Protein 7
IHC	Immunohistochemistry
IL	Interleukin
IMC	Imaging Mass Cytometry
imtCAF	Immortalized Cancer-Associated Fibroblast
INHBA	Inhibin Subunit Beta A
INV	Involucrin
ITG	Integrin
JAK	Janus Kinase
K	Keratin
KANK4	KN Motif and Ankyrin Repeat Domain-Containing Protein 4
KC	Keratinocyte
KEGG	Kyoto Encyclopedia of Genes and Genomes
KGF	Keratinocyte Growth Factor
LAMβ3	Laminin Subunit Beta-3
LOX	Lysyl Oxidase
LRIG1	Leucine-Rich Repeats and Immunoglobulin-Like Domains 1
LRRC15	Leucine-Rich Repeat Containing 15
LUM	Lumican
Ly6C	Lymphocyte Antigen 6 Complex, Locus C
MAP	Mitogen-Activated Protein
MC	Melanocyte
MCAM	Melanoma Cell Adhesion Molecule
MDSC	Myeloid-Derived Suppressor Cell

MEOX	Mesenchyme Homeobox
MGP	Matrix Gla Protein
MHC	Major Histocompatibility Complex
MITF	Microphthalmia-Associated Transcription Factor
MMP	Metalloproteinase
MOI	Multiplicity of Infection
mTOR	mammalian Target of Rapamycin
MYH11	Myosin Heavy Chain 11
NF	Normal Fibroblast
NFκB	Nuclear Factor Kappa B
NHEK	Normal human epidermal keratinocyte
NHS	Normal Human Serum
NK	Natural Killer
NP	Nanoparticle
NSCLC	Non-Small Cell Lung Cancer
NTN1	Netrin-1
OS	Overall Survival
P/S	Penicillin/Streptomycin
PANC	Pan-keratin
PDI	Polydispersity Index
PDGFα	Platelet-Derived Growth Factor Alpha
PD1	Programmed Cell Death Protein 1
PDL	Programmed Death Ligand
PDPN	Podoplanin
PEDF	Pigment Epithelium–Derived Factor
PEG	Polyethylene Glycol
PF	Papillary fibroblast
PI	Propidium Iodide
PI3K	Phosphoinositide 3-Kinase
PLGA	Poly(lactic-co-glycolic acid)
PMA	Phorbol 12-myristate 13-acetate
POSTN	Periostin
PPARγ	Peroxisome Proliferator-Activated Receptor Gamma
PSC	Pancreatic Stellate Cell

PSG1	Pregnancy-Specific Glycoprotein 1
PTGES2	Prostaglandin E Synthase 2
PTX	Paclitaxel
PVDF	Polyvinylidene Difluoride
PVA	Polyvinyl Alcohol
RGS5	Regulator of G Protein Signaling 5
RHE	Reconstructed Human Epidermis
RIPA	Radioimmunoprecipitation Assay
RF	Reticular fibroblast
ROCK	Rho-Associated Coiled-Coil Containing Protein Kinase
ROS	Reactive Oxygen Species
RPS29	Ribosomal Protein S29
SA-β-Gal	Senescence-Associated Beta-Galactosidase
SAHA	Suberoylanilide Hydroxamic Acid (Vorinostat)
SAP	Superabsorbent Polymer
SASP	Senescence-Associated Secretory Phenotype
SCA1	Stem Cell Antigen-1
SC	Single-Cell
SD	Standard Deviation
SDHA	Succinate Dehydrogenase Complex Subunit A
SKCM	Cutaneous Melanoma
SMO	Smoothened, Frizzled Class Receptor
SOX10	SRY-Box Transcription Factor 10
SPARC	Secreted Protein Acidic and Rich in Cysteine
SPP1	Secreted Phosphoprotein 1
SPRR2A	Small Proline-Rich Protein 2A
STAT	Signal Transducer and Activator of Transcription
TAGLN	Transgelin
TAEC	Tumor-Associated Endothelial Cell
TAM	Tumor-Associated Macrophage
TAN	Tumor-Associated Neutrophil
TBP	TATA-Box Binding Protein
TGFβ	Transforming Growth Factor-Beta
TGM2	Transglutaminase-2

TEM	Transmission Electron Microscopy
TIMP	Tissue Inhibitor of Metalloproteinase
TMEM200A	Transmembrane Protein 200A
TME	Tumor Microenvironment
TNC	Tenascin-C
TNFRSF	Tumor Necrosis Factor Receptor Superfamily
Treg	Regulatory T
TSP1	Thrombospondin-1
TYR	Tyrosinase
uPA	Urokinase-Type Plasminogen Activator
UV (R)	Ultraviolet (Radiation)
VCAM	Vascular Cell Adhesion Molecule
VCAN	Versican
VEGF	Vascular Endothelial Growth Factor
VIM	Vimentin
VPA	Valproic Acid
vSCC	Vulvar Squamous Cell Carcinoma
VWA5A	Von Willebrand Factor A Domain–Containing Protein 5A
ZEB	Zinc Finger E-Box–Binding
ZNF410	Zinc Finger Protein 410

List of publications

Leading projects:

1. **Shidi Wu**, Rui Fang, Marion H. Rietveld, Jeroen R.G. Torremans, Yang Liu, Zili Gu,Jan N. Bouwes Bavinck, Maarten H. Vermeer and Abdoelwaheb El Ghalbzouri. Identification of Small-Molecule Inhibitors Targeting Different Signaling Pathways in Cancer-Associated Fibroblast Reprogramming under Tumor-Stroma Interaction. *J Invest Dermatol. 2025 Jan;145(1):65-76.e13.*

2. Yuanyuan He*****, **Shidi Wu***, Marion Rietveld, Maarten Vermeer, Luis J Cruz, Christina Eich and Abdoelwaheb El Ghalbzouri. Application of Doxorubicin-Loaded PLGA Nanoparticles Targeting Both Tumor Cells and Cancer-Associated Fibroblasts on 3D Human Skin Equivalents Mimicking Melanoma and Cutaneous Squamous Cell Carcinoma. *Biomater Adv. 2024 Jun;160:213831.* (co-first authorship)

3. **Shidi Wu***, Bertine W. Huisman*, Marion H. Rietveld, Robert Rissmann, Maarten H. Vermeer, Mariette I. E. van Poelgeest and Abdoelwaheb El Ghalbzouri. The Development of in vitro Organotypic 3D Vulvar Models to Study Tumor-Stroma Interaction and Drug Efficacy. *Cell Oncol. 2024 Jun;47(3):883-896.* (co-first authorship)

4. Fangqi Chen*****, **Shidi Wu***, Jinshan Zhan, Yifan Jin, Xiuyun Xuan, Juanmei Cao, Ting Wu, Yan Liang, Xiaoqian Zhao, Zhiyan Li, Yuqing Wang, Li Chen, Yanqiu Li, Abdoelwaheb El Ghalbzouri and Changzheng Huang. IL-22-Induced Ubiquitin-specific Protease 15 Promotes Proliferation and Inflammation of Keratinocytes via Stabilization of SCCA2. *J Invest Dermatol. 2024 Jan;144(1):63-72.e4.* (co-first authorship)

5. **Shidi Wu**, Marion Rietveld, Marieke Hogervorst, Frank de Gruijl, Sjoerd van der Burg, Maarten Vermeer, Remco van Doorn, Marij Welters and Abdoelwaheb El Ghalbzouri. Human Papillary and Reticular Fibroblasts Show Distinct Functions on Tumor Behavior in 3D-Organotypic Cultures Mimicking Melanoma and HNSCC. *Int J Mol Sci. 2022 Oct 1;23(19):11651.*

6. Ting Wu*, **Shidi Wu***, Ling-yun Zhang, Hai-hua Ye, Ye-hong Mao, Xin Lian, Juan Tao, Chang-zheng Huang, Jing-si Zeng. Pathogen analysis of superficial mucocutaneous mycosis in Central China from 2007-2018**.** *Curr Med Sci. 2022 Apr;42(2):434-438.* (co-first authorship)

7. **Wu S**, Zhao M, Sun Y, Xie M, Wu T, Le K, Xu M, Huang C. The potential of Diosgenin in treating psoriasis: Studies from HaCaT keratinocytes and imiquimod-induced murine model. *Life Sci. 2020. 241C (2020) 117115.*

Collaborative projects:

1. Ye Zeng[#]*, Gangyin Zhao[#], **Shidi Wu**, Bochuan, Hu, Gabriel Forn-Cuní, Renzo Knol, Abdoelwaheb El Ghalbzouri, Ewa Snaar-Jagalska*, and Alexander Kros*. CD44-Targeted Lipid Nanoparticles for Enhanced CRISPR-Cas9 Delivery in Cancer Gene Editing**.** *J Controlled Release. 2026. https://doi.org/10.1016/j.jconrel.2025.114598*

2. Tim van Groningen, **Shidi Wu**, Joel Ruegger, Roderick Slieker, Arend Boogaard, Inger Kreuger, Sanne de Haan, Elisa Arlotti, Oren Lapid, Aart Jochemsen, Sarantos Kostidis, Marieke van de Ven, Natalie Proost, Serge Zander, Peter de Keizer, Martin Giera, Abdoel El Ghalbzouri, Elena Sanchez Lopez, Mario van der Stelt, Remco van Doorn*. Elimination of senescent cells through ferroptosis as a treatment strategy for congenital melanocytic nevus. (Submitted)

Curriculum Vitae

Shidi Wu was born on September 13, 1994, in Hubei Province, China. During his three years of high school education at the No.2 Senior High School of Huangshi, Hubei Province (HSEZ), he developed a strong interest in the natural science subjects, especially in Biology. Thereafter, he started his medical studies and obtained his Bachelor's degree in Medicine from Hubei University of Medicine in June 2017, graduating with the highest honors. During his undergraduate studies, he spent six months in Sydney, Australia, where he participated in a fundamental research project on Doxorubicin-induced cardiotoxicity at the Bosch Institute, The University of Sydney, under the supervision of Dr. Donna Lai. In his final year of hospital internship, he developed a strong interest in Dermatology.

Following his graduation, he continued his medical studies as a Master student in Dermatology and Venereology at Tongji Medical School, Huazhong University of Science and Technology, in Wuhan, China, from September 2017 to June 2020. Under the supervision of Prof. Dr. Changzheng Huang, his research focused on identifying novel pharmacological compounds for treating psoriasis and investigating ubiquitination in the progression of the disease.

In December 2020, Shidi began his PhD at Leiden University Medical Center in the Netherlands, under the supervision of Prof. Dr. Maarten Vermeer and Dr. Abdoelwaheb El Ghalbzouri in the Department of Dermatology. His doctoral research focused on developing advanced 3D skin models to investigate tumor-stroma interactions and evaluate therapeutic efficacy.

Currently, Shidi is continuing his research as a Postdoctoral Fellow in the same group, focusing on skin model valorization as part of the NGID grant initiative. His work aims to bridge the gap between fundamental research and clinical applications by advancing the development of innovative 3D skin models for dermatological research and the validation of therapeutic interventions.

Acknowledgments

Completing my PhD has been a journey filled with challenges, growth, and unforgettable experiences. This achievement would not have been possible without the guidance, support, and encouragement of many individuals, to whom I extend my deepest gratitude.

First and foremost, I would like to extend my heartfelt appreciation to my supervisors, Prof. Dr. Maarten Vermeer and Dr. Abdoelwaheb El Ghalbzouri. Your unwavering support, insightful discussions, and constructive feedback have been invaluable throughout my PhD. Maarten, your vast knowledge and scientific rigor have significantly shaped my research approach and critical thinking. Abdoel, your encouragement and guidance in the field of skin biology and 3D tissue engineering have been truly inspiring and largely shaped my future scientific interests. Most importantly, thank you for being both a mentor and a friend. I appreciate your belief in me and the environment you created in which I could grow both scientifically and personally.

I am also grateful to all my lab members in the Department of Dermatology at LUMC. The collaborative and supportive atmosphere in the lab made even the most challenging moments manageable. Your technical support, stimulating discussions, and the shared laughter during experiments have made my time in the lab a memorable experience.

A special word of thanks to my collaborators, whose expertise and contributions have greatly enriched my research. I sincerely appreciate your time, resources, and valuable insights that have helped bring this project to completion.

To all my friends, both near and far, thank you for being my pillars of support. Your companionship, laughter, the venting sessions, and moments of joy have made this PhD journey so much more meaningful. Whether it was sharing a coffee break, offering words of encouragement, or simply being there when I needed a break, I am genuinely grateful for your presence in my life. To my dearest boyfriend Marcel, your love, patience, and constant encouragement have been my source of strength during the most difficult times. Thank you for always being there, for celebrating my achievements, and for lifting me up when I needed it the most. I love you.

Finally, to my parents, my eternal safe harbor, words cannot express my gratitude for your unconditional love and support. You have always believed in me and encouraged me to follow my dreams, no matter how far they took me. Your sacrifices and unwavering faith in me have been my greatest motivation. 致所有至明和至暗的时刻，致你们所给予我的全部，

致我们与彼此的温柔连结，致爱与永恒。(Translation: To every moment, luminous and shadowed alike to all that you have bestowed upon me; to the tender connections that bind us to one another; to love, and to the everlasting.)

This PhD thesis is not just my accomplishment but a reflection of the collective support, inspiration, and kindness I have received from all of you. Thank you from the bottom of my heart.