



Universiteit
Leiden
The Netherlands

Nanoparticle-based combination drug delivery systems for effective cancer treatment

He, Y.

Citation

He, Y. (2024, June 25). *Nanoparticle-based combination drug delivery systems for effective cancer treatment*. Retrieved from <https://hdl.handle.net/1887/3765914>

Version: Publisher's Version

License: [Licence agreement concerning inclusion of doctoral thesis in the Institutional Repository of the University of Leiden](#)

Downloaded from: <https://hdl.handle.net/1887/3765914>

Note: To cite this publication please use the final published version (if applicable).

Appendix

List of abbreviations

List of publications

Curriculum vitae

Acknowledgement

List of abbreviations

ANOVA	Analysis of variance
BSA	Bovine serum albumin
CaCl ₂ 2H ₂ O	Calcium chloride dihydrate
CAFs	Cancer-associated fibroblasts
CaF ₂	Calcium fluoride
CLSM	Confocal laser scanning microscopy
Cer	Ceramide
cSCC	Cutaneous squamous cell carcinoma
CXCL12	C-X-C motif chemokine 12
DAPI	4',6-Diamidino-2-phenylindole
DHA	Docosahexaenoic acid
DLS	Dynamic light scattering
DMSO	Dimethyl sulfoxide
DMEM	Dulbecco's modified eagle medium
DMF	Dimethylformamide
DOX	Doxorubicin
Doxil	Liposomal doxorubicin
ECM	Extracellular matrix,
EGF	Epidermal growth factor
EGFR	Epidermal growth factor receptor
ELISA	Enzyme-linked immunosorbent assay
EMT	Epithelial–mesenchymal transition
Em	Emission
ER α	Estrogen receptor alpha
ERBB2	Epidermal growth factor 2
ERK5	Extracellular-regulated protein kinase 5
Er α	Estrogen receptor alpha

Ex	Excitation
FA	Fatty acids
FA	Folic acid
FBS	Fetal bovine serum
FCS	Fetal calf serum
FDA	Food and Drug Administration
FITC	Fluorescein isothiocyanate
FTM	Full-thickness model
GBM	Glioblastoma multiforme
Gd ³⁺	Gadolinium
HAI	Histological Alteration Index.
H ₂ O	Water
H&E	Hematoxylin and eosin
HMGA2	High-mobility group AT-hook 2
HSE	Human skin equivalent
IC50	Half maximal inhibitory concentration
ICD	Immunogenic cell death
IFNs	Interferons
IFN- γ	Interferon gamma
IRFs	Interferon regulatory factors
LAS X	Leica Application Suite X
LD	Light/dark
LPS	Lipopolysaccharide
LUMC	Leiden University Medical Center
Man MPs	Mannose-modified macrophage-derived microparticles
ManNP	Mannosylated cationic nano hydrogel particles
Met	Metformin
MGL	Macrophage galactose-specific C-type lectin

MMP	Matrix metalloproteinase
MSCs	Mesenchymal stem cells
MSV	Multistage nanovectors
MSNs	Mesoporous silica nanoparticles
MTS	3- (4,5-Dimethylthiazol-2-yl)-5- (3-carboxymethoxyphenyl)-2- (4-sulphophenyl)-2H-tetrazolium
MTX	Methotrexate
MWCNTs	Multi-walled carbon nanotubes
Nd ³⁺	Neodymium
NH ₄ F	Ammonium fluoride
NIR	Near-infrared
NPs	Nanoparticles
NSCLC	Non-small-cell lung cancer
PA	Palmitic acid
PBS	Phosphate-buffered saline
PDI	Polydispersity index
PEG	Polyethylene glycol
PEI	Polyethylenimine
PFA	Paraformaldehyde
PGA	Polyglycolic acid
PHA	PEG-histidine-modified alginate
PI3K	Phosphatidylinositol 3 kinase
PIGF	Placental growth factor
PLGA	Poly (lactic-co-glycolic acid)
PLA	Polylactic acid
PS	Polystyrene
PV	Perivascular
PVA	Polyvinyl alcohol
RENPs	Rare-earth doped nanoparticles

RES	Reticuloendothelial system
RIPA	Radioimmunoprecipitation assay
RKIP	Raf kinase inhibitor protein
RT	Room temperature
SD	Standard deviation
SEM	Standard error of the mean
SF	Serum-free
SKCM	Specifically cutaneous melanoma
SM	Sphingomyelin
SOX10	SR _Y (sex determining region Y)-related HMG-box 10
SR-B1	Scavenger receptor B type 1
STAT	Signal transducer and activator of transcription proteins
TAMM	TAM membrane
TEM	Transmission electron microscope
TiO ₂	Titanium dioxide
TME	Tumor microenvironment
TLR	Toll-like receptors
UCNPs	Upconversion NPs
UPLS-MS	Ultraperformance liquid chromatography-tandem mass spectrometry
W ₁ /O	Water-in-oil
W ₁ /O/W ₂	Water-in-oil-in-water
XRD	X-ray Diffractogram
Y ³⁺	Ytterbium
λ _{em}	Emission maximum
λ _{ex}	Excitation maximum

List of publications

1. **He, Y.**; Wu, S.; Rietveld, M.; Vermeer, M.; Cruz, L.J.; Eich, C.; El Ghalbzouri, A. 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. *Biomaterials Advances* 2024, 160, 213831, doi:<https://doi.org/10.1016/j.bioadv.2024.213831>.
2. **He, Y.**; de Araújo Júnior, R.F.; Cavalcante, R.S.; Yu, Z.; Schomann, T.; Gu, Z.; Eich, C.; Cruz, L.J. Effective breast cancer therapy based on palmitic acid-loaded PLGA nanoparticles. *Biomaterials Advances* 2023, 145, doi:[10.1016/j.bioadv.2022.213270](https://doi.org/10.1016/j.bioadv.2022.213270).
3. **He, Y.**; Yu, Z.; Schomann, T.; Zhang, H.; Eich, C.; Cruz, L.J. An EGF-modified PLGA-lanthanide nanoplatform for combined NIR-II cancer imaging and targeted drug delivery. *bioRxiv* 2023, 10.1101/2023.06.18.545497, doi:[10.1101/2023.06.18.545497](https://doi.org/10.1101/2023.06.18.545497).
4. Hao, Y.; Ma, S.; Gu, Z.; Haghparast, A.; Schomann, T.; Yu, Z.; **He, Y.**; Dong, X.; Cruz, L.J.; Ten Dijke, P. Combination of photodynamic therapy and stimulator of interferon genes (STING) agonist inhibits colorectal tumor growth and recurrence. *Cancer Commun (Lond)* 2023, 10.1002/cac2.12405, doi:[10.1002/cac2.12405](https://doi.org/10.1002/cac2.12405).
5. **He, Y.**; Rezaei, S.; Júnior, R.F.d.A.; Cruz, L.J.; Eich, C. Multifunctional Role of Lipids in Modulating the Tumorigenic Properties of 4T1 Breast Cancer Cells. *International Journal of Molecular Sciences* 2022, 23, doi:[10.3390/ijms23084240](https://doi.org/10.3390/ijms23084240).
6. Yu, Z.; **He, Y.**; Schomann, T.; Wu, K.; Hao, Y.; Suidgeest, E.; Zhang, H.; Eich, C.; Cruz, L.J. Achieving Effective Multimodal Imaging with Rare-Earth Ion-Doped CaF₂ Nanoparticles. *Pharmaceutics* 2022, 14, doi:[10.3390/pharmaceutics14040840](https://doi.org/10.3390/pharmaceutics14040840).
7. Yu, Z.; **He, Y.**; Schomann, T.; Wu, K.; Hao, Y.; Suidgeest, E.; Zhang, H.; Eich, C.; Cruz, L.J. Rare-Earth-Metal (Nd (3+), Ce (3+) and Gd (3+))-Doped CaF (2): Nanoparticles for Multimodal Imaging in Biomedical Applications. *Pharmaceutics* 2022, 14, doi:[10.3390/pharmaceutics14122796](https://doi.org/10.3390/pharmaceutics14122796).

8. **He, Y.**; de Araujo Junior, R.F.; Cruz, L.J.; Eich, C. Functionalized Nanoparticles Targeting Tumor-Associated Macrophages as Cancer Therapy. *Pharmaceutics* 2021, 13, 50, doi:10.3390/pharmaceutics13101670.
9. Dong, X.; Zeng, Y.; Zhang, Z.; Fu, J.; You, L.; **He, Y.**; Hao, Y.; Gu, Z.; Yu, Z.; Qu, C., *et al.* Hypericin-mediated photodynamic therapy for the treatment of cancer: a review. *J Pharm Pharmacol* 2021, 73, 425-436, doi:10.1093/jpp/rgaa018.
10. **He, Y.**; Wang, Y.; Zhang, H.; Zhang, Y.; Quan, F. Alpha-lipoic acid improves the maturation and the developmental potential of goat oocytes *in vitro*. *Reprod Domest Anim* 2021, 56, 545-554, doi:10.1111/rda.13892.
11. **He, Y.**; Meng, K.; Wang, X.; Dong, Z.; Zhang, Y.; Quan, F. Comparison of Bovine Small Antral Follicle Development in Two- and Three-Dimensional Culture Systems. *An Acad Bras Cienc* 2020, 92, e20180935, doi:10.1590/0001-3765202020180935.
12. Meng, K.; Wang, X.; **He, Y.**; Yang, J.; Wang, H.; Zhang, Y.; Quan, F. The Wilms tumor gene (WT1) (+/-KTS) isoforms regulate steroidogenesis by modulating the PI3K/AKT and ERK1/2 pathways in bovine granulosa cells. *Biol Reprod* 2019, 100, 1344-1355, doi:10.1093/biolre/ioz003.
13. Meng, K.; Wang, X.; **He, Y.**; Wang, H.; Xie, X.; Zhang, Y.; Quan, F. Evidence that downregulation of Wilms' tumor 1 (WT1) is involved in cortical stromal cell differentiation into theca cells in adult bovine ovaries. *Molecular Reproduction and Development* 2019, 86, 1731-1740.
14. Wang, X.; Meng, K.; **He, Y.**; Wang, H.; Zhang, Y.; Quan, F. Melatonin Stimulates STAR Expression and Progesterone Production via Activation of the PI3K/AKT Pathway in Bovine Theca Cells. *Int J Biol Sci* 2019, 15, 404-415, doi:10.7150/ijbs.27912.
15. Wang, X.; Zou, P.; **He, Y.**; Meng, K.; Quan, F.; Zhang, Y. Effect of luteinizing hormone on goat theca cell apoptosis and steroidogenesis through activation of the PI3K/AKT pathway. *Animal reproduction science* 2018, 190, 108-118.

Curriculum Vitae

Yuanyuan He was born on September 8, 1990, in Henan Province, China. In 2011, she was admitted to Henan University of Science and Technology, where she pursued a major in Animal Medicine. She successfully obtained a Bachelor's degree in Agriculture in 2015. Following this, she embarked on her master's degree in Embryo Engineering at the Key Laboratory of Animal Biotechnology (Ministry of Agriculture) at Northwest A&F University. During her master's program, she worked under the guidance of Fusheng Quan. Her research interests primarily lie in the field of reproductive physiology and germ cell signaling mechanisms. Her work encompasses various areas, such as comparing follicular development and culture systems, exploring the hormonal effects on ovarian cell function, and investigating the regulation of granulosa cell function by the WT1 gene.

In 2018, she commenced her Ph.D. research at Leiden University Medical Center in the Netherlands. She had the privilege of being supervised by esteemed professionals, namely Prof. Mark A. van Buchem, Dr. Luis J. Cruz, and Dr. Christina Eich. Throughout her doctoral studies, Yuanyuan focused on tumor immunology, delving into critical aspects such as immunomodulation of the tumor microenvironment, tumor immunochemotherapy, and the targeted delivery of nanomedicines.

Acknowledgment

The completion of this thesis unites a special period of scientific research filled with professional and personal challenges. I would like to express my deepest gratitude to all those involved during this period.

To my promotor, Prof. Mark van Buchem, I want to express my sincerest gratitude for your unwavering support and assistance during my PhD studies. Your guidance and mentorship have been invaluable in shaping my research and academic journey, and I am truly grateful for your dedication and commitment.

To my supervisors, Dr. Luis Cruz and Dr. Christina Eich, I would like to express my deep gratitude for your supervision and guidance. Your expertise and insightful feedback have played a crucial role in shaping the direction of my work. I sincerely appreciate your patience, encouragement, and continuous trust in my abilities. Dr. Luis Cruz's profound knowledge in nanotechnology and his insights into the field of nanomedicine are commendable. I am honored to have had the opportunity to explore the mysteries of nanomedicine under his guidance. His expertise has enabled me to understand complex concepts and technologies and apply them in my research. Dr. Christina Eich's rigorous research attitude and insightful perspectives have provided valuable guidance and inspiration for me in exploring every question. Her profound professional knowledge has allowed me to grasp complex concepts and technologies and apply them in my research. I am particularly grateful for Dr. Christina Eich's generosity and kindness, and her assistance and encouragement have helped me overcome challenges and difficulties in my research.

I am deeply grateful to my paranymphs, Shidi and Claudia, for their companionship and friendship throughout our journey together. We have shared many wonderful moments and formed a strong bond. Your presence has enriched my research and life, creating cherished memories.

Many thanks to all members of our research team, especially Timo, Raimundo, Somayeh, Sana, Jelle, Eric, Gaston, Ruben, Candido, Sabine, Ivo, Pablo, Carla, Julio, Andy, Ana Luiza, Filippo, Fabio, Chih Kit, Olena, Dong Xiaoxu, Rômulo, for their collaborative efforts and technical assistance. Their dedication and contributions contributed significantly to the success of this project. I thank them for their insightful discussions, shared expertise, and friendship.

Many thanks to my dearest friends, Yiyi, you have been like a ray of light shining

into my life. Thank you for your unwavering support even before we met face-to-face, for picking me up at the airport when I first arrived in the Netherlands, for your support during work, and for your companionship in daily life! We have shared many wonderful moments together and formed a deep friendship. Many thanks to beloved Yang, for your invaluable assistance whenever I encountered difficulties in work and life. Many thanks lovely Zili, for sharing various culinary delights and research experiences. Many thanks to kind-hearted Yixin and Yijing, for your timely support and treats. Many thanks to humble gentleman Ma sen, for your prompt assistance during experiments. Many thanks to warm-hearted Yumeng, for always providing timely advice and help. Many thanks to lovely Jinqiu, for showing me the liveliness of Leiden's open market and the Dutch way of life. You are like angels, and with your presence, you have added many wonderful memories to my research and life.

I would like to express my deepest gratitude to my husband, Zhihang Dong, for his unwavering support, understanding, and encouragement throughout this journey. You are the solid pillar in my life, and it is with your support that I am able to focus on my passions and aspirations. I am truly fortunate to have you by my side! In addition, I would like to express my gratitude to my family for their love, trust in me, and understanding of the challenges I face. Their love and support have been a constant source of motivation for me to keep moving forward.

While I am deeply thankful to all the individuals mentioned, I also acknowledge that this expression of gratitude may not include everyone who has contributed to my research in some way. To those whose names may have inadvertently been omitted, please accept my heartfelt gratitude for your support and help.