

Nanoparticle-based combination drug delivery systems for effective cancer treatment He. Y.

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Appendix

List of abbreviations
List of publications
Curriculum vitae
Acknowledgement

List of abbreviations

ANOVA Analysis of variance

BSA Bovine serum albumin

CaCl₂ 2H₂O Calcium chloride dihydrate

CAFs Cancer-associated fibroblasts

CaF₂ 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

ERα Estrogen receptor alpha

ERBB2 Epidermal growth factor 2

ERK5 Extracellular-regulated protein kinase 5

Erα Estrogen receptor alpha

Ex Exitation

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

Gd³⁺ Gadolinium

HAI Histological Alteration Index.

H₂O 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-carboxymethophenyl)-2- (4-sul-

fophenyl)-2H-tetrazolium

MTX Methotrexate

MWCNTs Multi-walled carbon nanotubes

Nd³⁺ Neodymium

NH₄F Ammonium fluoride

NIR Near-infrared

NPs Nanoparticles

NSCLC Non-small-cell lung cancer

PA Palmitic acid

PBS Phosphate-muffered 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 SRY (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

TiO₂ Titanium dioxide

TME Tumor microenvironment

TLR Toll-like receptors

UCNPs Upconversion NPs

UPLS-MS Ultraperformance liquid chromatography-tandem mass spectrometry

W₁/O Water-in-oil

W₁/O/W₂ Water-in-oil-in-water

XRD X-ray Diffractogram

Y³⁺ Ytterbium

λem Emission maximum

λex Exitation maximum

List of publications

- 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.
- 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.
- 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.
- 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.
- 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.
- 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.
- 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.

- 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.
- 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.
- 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.
- 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 cellsdagger. 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.
- 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.

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