



Universiteit
Leiden
The Netherlands

Photodynamic therapy-based combinations with immunotherapy in colon cancer treatment

Hao, Y.

Citation

Hao, Y. (2023, January 18). *Photodynamic therapy-based combinations with immunotherapy in colon cancer treatment*. Retrieved from <https://hdl.handle.net/1887/3511806>

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/1887/3511806>

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

Curriculum Vitae

Yang Hao was born on Oct. 23, 1993, in Jilin Province, China. In 2015, Yang received her Bachelor of Science degree in Animal Science at Jilin University, Jilin Province, China. In 2015, she started her master's study at Jilin University under the supervision of Dianfeng Liu and Dongxu Wang. She studied the molecular mechanism of action of small molecule drugs in cancer therapy. In 2018, Yang received her Master of Science degree in Zoology and Yang started her Ph.D. study funded by the China Scholarship Council at the Department of Cell Chemical Biology at the Leiden University Medical Center. During that period, she studied long noncoding RNAs that promote TGF- β pathway-associated breast cancer metastasis under the supervision of Prof. Peter ten Dijke. In 2019, Yang shifted focus towards obtaining new insights in nanotechnology-supported photodynamic therapy in combination with other therapeutic strategies in cancer treatment. This research was performed under the direct supervision of Dr. Luis J Cruz at the Department of Radiology.

List of publications

Publications with LUMC, Leiden, The Netherlands affiliation:

1. **Hao Y.**, Ma S, Gu Z, Haghpour A, Schomann T, Yu Z, He Y, Dong X, Cruz LJ, Ten Dijke P. Combination of Photodynamic Therapy and STING Agonist Efficiently Eradicates Established Colorectal Tumors *Cancer Communications* (accepted)
2. **Hao Y**, Chung CK, Gu Z, et al. Combinatorial therapeutic approaches of photodynamic therapy and immune checkpoint blockade for colon cancer treatment. *Mol Biomed*. 2022;3(1):26.
3. **Hao, Y.**, Gu Z, Yu Z, Schomann T, Sayedipour S, Aguilar JC, Ten Dijke P, Cruz LJ. Photodynamic Therapy in Combination with the Hepatitis B Core Virus-like Particles (HBc VLPs) to Prime Anticancer Immunity for Colorectal Cancer Treatment. *Cancers*. 2022;14(11):2724.
4. **Hao Y**, Chung CK, Yu Z, et al. Chung CK, Yu Z, Huis In 't Veld RV, Ossendorp FA, Ten Dijke P, Cruz LJ. Combinatorial Therapeutic Approaches with Nanomaterial-Based Photodynamic Cancer Therapy. *Pharmaceutics*. 2022;4;14(1):120.
5. Yu Z, He Y, Schomann T, Wu K, **Hao Y**, Suidgeest E, Zhang H, Eich C, Cruz LJ. Achieving Effective Multimodal Imaging with Rare-Earth Ion-Doped CaF₂ Nanoparticles. *Pharmaceutics*. 2022;11;14(4):840.
6. Cai M, Zeng Y, Liu M, You L, Huang H, **Hao Y**, Yin X, Qu C, Ni J, Dong X. Construction of a Multifunctional Nano-Scale Metal-Organic Framework-Based Drug Delivery System for Targeted Cancer Therapy. *Pharmaceutics*. 2021;17;13(11):1945.
7. Dong X, Zeng Y, Zhang Z, Fu J, You L, He Y, **Hao Y**, Gu Z, Yu Z, Qu C, Yin X, Ni J, Cruz LJ. Hypericin-mediated photodynamic therapy for the treatment of cancer: a review. *J Pharm Pharmacol*. 2021;73(4):425-436.
8. **Hao, Y.**, Baker D, Ten Dijke P. TGF- β -Mediated Epithelial-Mesenchymal Transition and Cancer Metastasis. *Int J Mol Sci*. 2019;20(11):2767.

Publications with Jilin University, Changchun, China affiliation:

1. Hao J, Li C, Lin C, **Hao, Y.**, Yu X, Xia Y, Gao F, Jiang Z, Wang D. Targeted point mutations of the m6A modification in miR675 using RNA-guided base editing induce cell apoptosis. *Biosci Rep*. 2020;40(5):BSR20192933.
2. Zhong X*, Liu D*, **Hao Y***, Li C, Hao J, Lin C, Shi S, Wang D. The expression of TET3 regulated cell proliferation in HepG2 cells. *Gene*. 2019;698:113-119.
3. Shen Z, Ma Y, Ji Z., **Hao, Y.**, Yan X, Zhong Y, Tang X, Ren W. Arachidonic acid induces macrophage cell cycle arrest through the JNK signaling pathway. *Lipids Health Dis*. 2018;17(1):26.
4. **Hao Y**, Wang G, Lin C, Li D, Ji Z, Gao F, Li Z, Liu D, Wang D. Valproic Acid Induces Decreased Expression of H19 Promoting Cell Apoptosis in A549 Cells. *DNA Cell Biol*. 2017;36(6):428-435.
5. Wang, D., Liu, Z., Yao, H., **Hao, Y.**, Zhou L, Du J, Zhu Y, Xu Y, Wang G, Song Y, Li Z. Disruption of NNAT, NAP1L5 and MKRN3 DNA methylation and transcription in rabbit parthenogenetic fetuses. *Gene*. 2017;626:158-162.

6. Wang D*, Wang G*, **Hao Y***, et al. DNA methylation modulates H19 and IGF2 expression in porcine female eye. *Genet Mol Biol.* 2017;40(1):153-159. doi: 10.1590/1678-4685-GMB-2016-0194
7. Ji, Z. H., Ren, W. Z., Gao, W., **Hao, Y.**, Gao W, Chen J, Quan FS, Hu JP, Yuan B. Analyzing the innate immunity of NIH hairless mice and the impact of gut microbial polymorphisms on *Listeria monocytogenes* infection. *Oncotarget.* 2017;8(63):106222-106232.

Acknowledgments

The path of pursuing a Ph.D. overseas is full of challenges. I am not grateful for the torture and hardship of life, but to myself, to fate, to the people that I met, and to all those I have to thank.

Thanks to Peter ten Dijke for the supervision and guidance. With his rigorous approach to learning, generous and benevolent heart, and optimistic attitude to life, Peter has set a lifelong example for me to follow. There are not only knowledge and research he taught me, the most precious is his trust which kept me from quitting my Ph.D.

Thanks to Luis J Cruz, I would like to express my sincere gratitude for the opportunities the group provided for me to be strong and independent. His strong expertise in nanotechnology and his academic insights encouraged me to explore nanomedicine in oncology.

Thanks to Ferry Ossendorp for his expertise in tumor immunology and meaningful discussions that benefited me a lot. I am greatly appreciative that he provided me with access to all the excellent research facilities, experimental models, and tools for immunological research.

Thanks to Kees Sier for his insightful research views, realistic attitude toward facts, and sharp and wise professional instincts. He showed me how to unlock life's chains and regain my motivation in my academic career. It was a great pleasure to be guided by you.

Thanks to Marcel for giving me practical help and teaching laboratory skills. He is the man who taught me the lab rules and always provided selfless help when I had difficulties.

Thanks to all those who have been kind and helpful, especially the colleagues of the Translational Nanobiomaterials and Imaging group, Alireza; Ana Luiza, Candido, Carla, Christina, Eric, Ivo, Pablo, Ruben, Sana, Somayeh, Timo; colleagues in CCB department, Baoxu Pang, Chao Li, Gerard, Jiang Ren, Jin Ma, Jing Zhang, Maarten, Midory, Sijia Liu, Yuqing Jia, Yufeng Li; and those that I have had the pleasure of being with, Brett, Koen, Marleen, Nannan Guo, Nelleke, Tamara, Xiaoke Ge, Xiaolin Meng, Yifan Zhu, Zhixiong Ying, Ziyang Shen, Zhou Zhou.

Thanks to my friends in China: Bozheng Li, Gaoxu Liu, Jiaqi Wei, Qingfeng Huang, Xinyu Zhang, Yuan Zhong, Yuwei Zhao, Zhenhua He, and Zhonghao Ji, League of Legends and those who have been my life in Leiden. Because of you, I consider myself the luckiest person on the face of the earth because of you. Thanks to Dongrun Wu, who makes the last days of my Ph.D. career count, wish you safe and brave, love life deeply and follow your heart; Lushun Yuan, who is a professional doctor, wish you success; Mingqi Zhang, I who teach me how to enjoy the vacation, wish you a colorful life and wonderful Love; Sheng Li, I am fortunate to have your complete logistic support in daily necessities, and wish you find someone that you're not settling for; Sen Ma, who is a delicate, sensitive and gentle man, wish you rich and determined; Xuefeng Guan, who is a big fan of games and Japanese anime, wish your future is bright; YuanYuan He, who provided me with a

lot of delicious food in daily life, wish you happy, and always being firmly chosen; Zhenfeng Yu, who enjoyed the crazy shopping with me, wish you innocent, unaffected, and always smile brilliantly; Zili Gu, who is the assistant on my way to graduation with her excellent experimental skills, wish you healthy.

Thanks to YuMeng Wang for giving me your hand, concern, support, and love, more precious than everything I gain in Netherlands! Thanks for understanding what I mean beyond words and for hesitating to say. You are my favorite hello and hardest goodbye. Wish you wealth and no longer trapped by reality, show me the money and smile! We'll always have Paris.

I would also like to thank my parents, Wangjie Yang and Tingsheng Hao. Thanks to their support in the completion of my Ph.D. life. They have always been supportive of my every rebellious decision. They embraced me and encouraged me with their tenderness, love and strength. In the days of my misfortune, they used the simplest but touching words to tell me "I love you, you will always be our treasure". I love you, too and you are all I've got.

Finally, may all your life be extraordinary and have no regrets.

List of abbreviations

ACQ	aggregation-caused quenching
AIE	aggregation-induced emission
ANOVA	analysis of variance
APCs	antigen-presenting cells
AQ4N	anoxantrone
ATP	adenosine triphosphate
AuNPs	gold nanoparticles
BCC	basal cell carcinoma
BDOX	anthracycline doxorubicin
BMDMs	bone marrow-derived macrophages
CaCO ₃	calcium carbonate
CBL	chlorambucil
CCM	cancer cell membrane
CSCs	cancer stem cells
CDs	carbon nanodots
CDDP	cisplatin
CDN	cyclic dinucleotides
c-di-AMP	cyclic di-adenosine monophosphate
c-di-GMP	cyclic dimeric guanosine monophosphate
c-GMP	cyclic guanosine monophosphate
CMFDA	5-chloromethylfluorescein diacetate
Col	collagenase
(COX)-2	cyclooxygenase-2
CP	conjugated polymer
CPNs	coordination polymer nanoparticles
CPT	camptothecin
CRC	colorectal cancer
CRT	calreticulin
CT	computed tomography
CTLs	cytotoxic T lymphocytes
CTLA-4	cytotoxic T-lymphocyte-associated protein 4
dsRNA	double-stranded RNA

dLNs	tumor-draining lymph nodes
DAMPs	damage-associated molecular patterns
DAPI	4',6-diamidino-2-phenylindole
DBCO	dibenzocyclooctyne
DCs	dendritic cells
DCFH-DA	2',7'-dichlorodihydrofluorescein diacetate
DMXAA	5,6-dimethylxanthenone-4-acetic acid
DOX	doxorubicin
DTX	docetaxel
ECM	extracellular matrix
ELISA	enzyme-linked immunosorbent assay
EMPD	extramammary paget's disease
EPR	enhanced permeability and retention
EQ4	apaziquone
FA	folic acid
FCS	fetal calf serum
FDA	U.S. food and drug administration
FL	fluorescent imaging
F/T	3 freeze/thaw cycle at -20 °C
gMFI	geometric mean fluorescence intensity
GM-CSF	granulocyte-macrophage colony-stimulating factor
GO	graphene oxide
GSH	glutathione
H ₂ O ₂	hydrogen peroxide
H ₂ O	water
HA	hyaluronic acid
HBcAg	hepatitis B core antigen
HBsAg	hepatitis B surface antigen
Hf	hafnium
HMGB1	high mobility group box 1
HSP	heat shock proteins
H&E	hematoxylin and eosin
IC ₅₀	half maximal inhibitory concentration
ICD	immunogenic cell death

ICG	indocyanine green
IDO	indoleamine 2,3-dioxygenase
IgG	immunoglobulin G
IFN	interferon
IL	interleukin
IPM-Br	bromoisophosphoramidate mustard intermediate
^{125}I	iodine-125
i.v.	intravenous
LPS	E. coli lipopolysaccharide
MDR	multi-drug resistance
MDSCs	myeloid-derived suppressor cells
MHC	major histocompatibility complex
MRI	magnetic resonance
MX	mitoxantrone
mTHPC	meta-tetrahydroxy-phenylchlorin
NLCs	nanosubstructured lipid carriers
NPs	nanoparticles
ODNs	oligodeoxynucleotides
OD	optical density
$\text{OH}^{\cdot}$	hydroxyl radicals
OXF	oxaliplatin
$\text{O}_2^{\cdot -}$	superoxide anions
$^3\text{O}_2$	triplet oxygen
$^1\text{O}_2$	singlet oxygen
PA	photoacoustic
PBS	phosphate-buffered saline
PDA	polydopamine
PDT	photodynamic therapy
PD-1	programmed cell death protein 1
PD-L1	programmed death ligand 1
PEG	polyethylene glycol
PET	positron emission tomography
PLA	polyglycolic acid
PLGA	poly(lactic-co-glycolic acid)

PNPs	polymeric nanoparticles
poly (I: C)	polyinosinic-polycytidylic acid
PS	photosensitizer
PS*	singlet or triplet state photosensitizer
Pt	platinum
RGD	arginylglycylaspartic acid
ROS	reactive oxygen species
RT	radiotherapy
SLNs	solid lipid nanoparticles
SLP	synthetic long peptides
SPIONs	superparamagnetic nanoparticles
STING	stimulator of interferon genes
SiO ₂	silica
TAA	tumor-associated antigens
TCPP	tetrakis(4-carboxyphenyl) porphyrin
TEM	transmission electron microscope
TLR	toll-like receptors
TME	tumor microenvironment
TNBC	triple-negative breast cancer
TNF	tumor necrosis factor
TPCS2a	meso-tetraphenyl chlorine disulfonate
TPZ	triapazamine
TiO ₂	titanium oxide
Tregs	regulatory T cells
UCNPs	up-conversion nanoparticles
VEGF	vascular endothelial growth
VP	verteporfin

