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## Optical imaging of cancer and cell death

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## **CHAPTER EIGHT**

### **Miscellaneous**



## Acknowledgements – 致谢 – Dankwoord

A past lecturer of Leiden University once said: If A is a success in life, then A equals X plus Y plus Z. Work is X; Y is play; and Z is keeping your mouth shut. That lecturer was later known world-wide as Albert Einstein. Attracted by the glory of numerous renowned scholars, I started working as a PhD candidate in Leiden University Medical Center four years ago. During the time I am pursuing my PhD, many people walked in and out of my life. When you read these lines, you must be one of them who have left footprints. Therefore, I will like to take this opportunity to thank you all!

Following the alphabetical order, I shall start from A, but since the time I started studying in University of Groningen, I realized the importance of “C” (Being a scientist, one needs to be Critical&Creative). So, please allow me to express my full gratitude first to Clemens Löwik for being my supervisor. From drafting the first paper to teach me canoeing in New Hampshire, the allocation of your time invested in me is tremendous and invaluable. Your full enthusiasm and creativity motivated me to keep going all the way. No matter what happens, you always guide me. You always know what direction to go, what to do and sometimes, also what to skip. Thank you so much for believing in me!

My two co-supervisors, Eric Kaijzel and Ermond van Beek, thank you for guiding me throughout the entire PhD study. Eric, I am grateful to receive your guidance on how to communicate with colleagues via emails and in person. Ermond, I learned so much from your critical point of view towards science and also your “rustig” style in life.

My two paronyms Laura Mezzanotte and Martijn Löwik, thank you very much for accompanying me in and out of the lab. Laura, thanks a lot for bringing your special Italian charm to the whole lab. It definitely spices up our days in the hospital. Martijn, supervising you in the lab is a pleasure, having you as a good friend is even more joyful.

I would like to personally thank other colleagues including, but not limited to: Ammar, Anna, Bart, Boudewijn, Dominique, Edwin, Ernst, Eugenio, Geertje, Guido, Henry, Isabel, Ineke, Jeroen, Jimmy, Judith, Jan-Willem, Jaap, Karien, Kassia, Kees, Luis, Louise, Lianne, Martijn V, Martiene, Man-Chi, Mieke, Marieke, Nancy, Patrick, Pieter D, Randa, Razvan, Trea, Thomas and Vicky. Special thanks go to Annelies, Chris, Frans, Hetty, Henny, Ivo and Joop for your constructive contributions to my PhD project. My appreciation goes to Danielle, Daniel and Bryan for your intensive and dedicated international collaborations.

I am indebted to Alan Chan for being a mentor, both at and outside our work. Thank you so much for infinitely guiding me to bridge the gap between Oriental and Western cultures! 多谢!

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I am very grateful to Prof. Dr. Pancras Hogendoorn from Leiden, for your hospitality to allocate your time in between your super-busy-Dean agenda. I would like to also thank Prof. Dr. Bauke Dijkstra, Dr. Anton Steen and Dr. Armagan Kocer from Groningen. Having a wise talk with each of you from time to time always brings me precious guidance that lasts long.

Titanic was a great ship, it sunk; the greatest ship is still Friendship. I feel blessed to have friends from all over the world. Please excuse me for not listing you guys, I am sorry, you are not on the list, but you are always in my heart. Each of you is like the star in the dark night. I can always find you when looking up to the sky, even though you are far away! Especially, I thank the great companionship of PJ and Moni, thank you two for your dedication to design such a wonderful thesis! Special thanks to Timmy's loyalty and my deep commemoration for Yingying.

流金岁月，似水年华；海外求学，四海为家。古有云：宝剑锋从磨砺出，梅花香自苦寒来。历经四百余年风霜，莱顿大学仍执许多科研领域之牛耳。我为自己能在莱顿大学医学院攻读博士感到自豪，也为在此期间能结识许多志同道合的朋友而倍感欣慰。君子之交淡若水，我就不再一一致谢了。细水长流，友谊常存。

我要感谢我的父母，感谢你们给予我健康的身体与善良的心智。请谅解我不能随时陪伴在你们左右，但无论天涯海角，你们都让我体会到什么是大爱无言，无国界。我爱你们！同时，我深深感谢在中国的每一位亲朋好友，尤其感谢年迈的长辈对我的记挂。你们莫大的关怀与挂念，是我一直勇往直前的动力。最后，我借此机会怀念我已逝去的至亲小姨和外公。

Being abroad six years, I worked my way up from the bottom. I thank all the friends I have met, you made the world more pretty; I also thank all the challengers I have met, you made me stronger to overcome difficulties and to appreciate the life I have been building up.

Lastly, back to the "C", I am proud to be an ordinary person coming from a most common Chinese family. As the ancient Chinese philosopher Mencius said: When a man is destined for a great responsibility, it first starts with frustration of his spirit and will, harassment by troubles and setbacks, so as to toughen his nature and enhance his abilities beyond the limit.

Alright, enough "C", the last one I would like to bring us all is "Celebration"!







## Curriculum Vitae

The author of this thesis was born in Jiangxi, China, on September 27<sup>th</sup>, 1985. After finishing high school, he moved from his hometown to Beijing in 2003. He enrolled in the four-year Bachelor programme in Biotechnology at Beijing University of Agriculture. There, he grounded himself in theories of Biotechnology and fundamental methodologies of biological research. He broadened his vision by participating in various extracurricular activities, including chairing the English student association in the university. In 2005, he represented the university to compete in China Central Television (CCTV) Cup National English Speaking Contest and won the Excellent Prize at the Provincial Final. His proficiency in English and his eager to learn more in Biomolecular research led him to challenge himself to study abroad.

In June 2007, the author obtained his Bachelor degree in Biotechnology and received full Scholarship to study the Top Master Programme in Biomolecular Sciences and Biotechnology at University of Groningen, The Netherlands. After attending intensive and multidisciplinary courses in Biomolecular Sciences, he started his first research internship at Membrane Enzymology group headed by Prof. Dr. Bert Poolman. Afterwards, he moved to Eindhoven to start his second internship at Biomolecular Engineering group in Philips Research Europe. Inspired by Dr. Marc Robillard, he discovered his great interest in Molecular Imaging.

After receiving a Top Master degree in Science in September 2009, he started pursuing his PhD, under the supervision of Prof. Dr. Clemens Löwik at Leiden University Medical Center (LUMC), The Netherlands. He was involved in the Center for Translational Molecular Medicine (CTMM) project entitled “Intra-operative Multi-Spectral Imaging Systems for Radical Tumor” (MUSIS), with a main research focus on non-invasive optical imaging of cancer and cell death. During the four-year PhD programme, he developed an international research network by actively collaborating with American, Australian and German research groups. For the research he conducted during his PhD, he received several honors and awards: a Young Investigator Award Nominee at the 8<sup>th</sup> European Molecular Imaging Meeting in 2013, Italy; a Travel Stipend Award at World Molecular Imaging Congress both in 2012, Ireland and in 2013, United States of America.

He will start working as a Post-doc researcher in October 2013 for a Marie Curie IAPP grant (project acronym: BRAINPATH), which has been awarded to a consortium of eight different European partners from industry and academia.

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## 作者简介

本论文作者一九八五年九月二十七日出生于中国江西省。他在二零零三年高中毕业后，离乡北上首都于北京农学院就读四年制生物技术学士课程。在那里，他夯实了自己在生物技术领域的理论基础，熟知了进行生物研究的基本方法。此外，通过参加各种课外活动，他开阔了视野，这其中包括了在大学期间担任院英语社学生协会主席。二零零五年，他代表了大学参加了“中国中央电视台(CCTV)杯”全国英语演讲比赛，并在决赛中获得了省级优秀奖。对英语的熟练掌握和对分子生物学进一步研究的渴求让他决定挑战自我，出国留学。

二零零七年六月，作者取得了生物技术学士学位并获得了在荷兰格罗宁根大学分子生物与生物技术系顶级硕士专业学习的全额奖学金。经过密集的分子生物多学科融合课程培训后，作者开始了他在以Bert Poolman 教授带领的膜酶学实验组的第一次研究实习。之后，他来到埃因霍温市飞利浦欧洲研发基地(Philips Research Europe)在分子生物工程组开始了他的第二次研究实习。在Marc Robillard 博士的启发之下，他对分子成像产生了极大的兴趣。

作者于二零零九年九月荣获顶级理学硕士学位，他继而在荷兰莱顿大学医学中心(LUMC) Clemens Löwik 教授的指导下开始攻读博士学位。他的博士项目隶属于荷兰临床分子医学转化中心(CTMM)旗下题为“手术中对肿瘤进行彻底切除的多光谱成像系统”(MUSIS)的科研项目，其研究的重点为对癌症和细胞死亡进行非侵入性光学成像。四年的博士学习，他通过积极地与美国、澳大利亚和德国的研究同仁合作，开拓了一个广阔的国际交流合作平台。博士期间，他获得多个荣誉和奖项：二零一三年第八届欧洲分子成像会议年度优秀青年研究者提名，二零一二年和二零一三年世界分子成像大会旅行津贴奖。

他将在二零一三年十月以博士后研究员身份加入居里夫人研究基金会旗下八个不同的欧洲产业界和学术界的合作伙伴组成的财团IAPP项目(项目代号: BRAINPATH)。

## Biografie

De auteur van dit proefschrift is op 27 september 1985 geboren in Jiangxi, China. Na het afronden van zijn middelbare school verhuisde hij naar Peking, alwaar hij het 4 jaar durende Bachelor programma in Biotechnologie heeft doorlopen aan de “Beijing University of Agriculture”. Daar heeft hij zich verdiept in de theoretische achtergrond van biotechnologie en fundamentele methodologieën van biologisch onderzoek. Hij verbreedde zijn visie door te participeren in diverse buitenschoolse activiteiten zoals onder andere het bekleden van het voorzitterschap van de Engelse Studenten Associatie binnen de universiteit. In 2005, vertegenwoordigde hij de Universiteit bij de wedstrijd uitgeschreven door China Central Television (CCTV) betreffende de best Engels sprekende student en won hij de “Excellent Prize” bij de provinciale finale. Zijn vaardigheid in het Engels en zijn gretigheid om meer te willen leren van biomoleculair onderzoek heeft er toe geleid dat hij graag de uitdaging aan wilde gaan om in het buitenland te studeren.

In Juni 2007, heeft de auteur zijn Bachelor graad gehaald in Biotechnologie en verwierf hij een volledige beurs om het Top Master Programma Biomoleculaire Wetenschappen en Biotechnologie in Groningen aan te vangen. Na het volgen van een aantal intensieve en multidisciplinaire cursussen in Biomoleculaire Wetenschappen, begon hij zijn eerste onderzoeksstage bij de Membraan Enzymologie groep van Prof. Dr. Bert Poolman. Hierna verhuisde hij naar Eindhoven om zijn tweede onderzoeksstage te beginnen bij de Biomoleculaire Engineerings groep binnen Philips Research Europe. Geïnspireerd door Dr. Marc Robillard, ontwikkelde hij een grote interesse voor Molecular Imaging.

Na het behalen van zijn “Top Master in Science” titel in september 2009, startte hij zijn promotieonderzoek onder leiding van Prof. Dr. Clemens Löwik binnen het Leids Universitair Medisch Centrum (LUMC). Hier was hij betrokken bij het “Center for Translational Molecular Medicine” (CTMM) project met de titel: “Intra-operative Multispectral Imaging Systems for Radical Tumor Resection”, of te wel het MUSIS project. Binnen dit project heeft de auteur zich bezig gehouden met non-invasieve optische beeldvorming van kankerweefsel en celdood in proefdieren. Tijdens zijn vierjarige promotietraject heeft hij een uitgebreid onderzoeksnetwerk ontwikkeld door intensief samen te werken met Amerikaanse, Australische en Duitse onderzoeksgroepen. Voor zijn promotieonderzoek verwierf hij verschillende onderscheidingen en prijzen zoals: Een “Young Investigator Nominee” op de achtste European Molecular Imaging Meeting in 2013 in Turijn; een “Travel Stipend Award” voor het “World Molecular Imaging Congress” voor zowel 2012 als 2013.

Vanaf oktober 2013 zal hij werkzaam zijn in het LUMC als post doc binnen het Europese Marie-Curie IAPP project met het acroniem “BRAINPATH” dat is toegekend aan een consortium van 8 verschillende Europese partners afkomstig uit de industrie en academische wereld.



## List of Publications

- Park D\*, **Xie BW\***, Van Beek ER, Blankevoort V, Que I, Löwik CW, Hogg PJ, Optical imaging of treatment-related tumor cell death using a heat shock protein-90 alkylator. *Mol Pharm*. 2013 Aug 22. [Epub ahead of print]
- **Xie BW\***, Park D\*, Van Beek ER, Blankevoort V, Orabi Y, Que I, Que I, Kaijzel EL, Chan A, Hogg PJ, Löwik CW, Optical imaging of cell death in traumatic brain injury using a heat shock protein-90 alkylator. *Cell Death Dis*. 2013; 4: e473.
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- Keereweer S, Kerrebijn JD, van Driel PB, **Xie BW**, Kaijzel EL, Snoeks TJ, Que I, Hutteman M, van der Vorst JR, Mieog JS, Vahrmeijer AL, van de Velde CJ, Baatenburg de Jong RJ, Löwik CW. Optical image-guided surgery--where do we stand? *Mol Imaging Biol*. 2011 Apr; 13(2):199-207.

\* = co-first authors