University of Groningen

Pex3-mediated peroxisomal membrane contact sites in yeast

Wu, Huala

DOI:
[10.33612/diss.113450193](https://doi.org/10.33612/diss.113450193)

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version
Publisher's PDF, also known as Version of record

Publication date:
2020

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):
Wu, H. (2020). *Pex3-mediated peroxisomal membrane contact sites in yeast*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.113450193>

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Pex3-mediated Peroxisomal Membrane Contact Sites in Yeast

Huala Wu

university of
 groningen

The research presented in this thesis was performed in the Molecular Cell Biology Group of the Groningen Biomolecular Sciences and Biotechnology Institute (GBB) of the University of Groningen, the Netherlands.

This project was supported financially by the China Scholarship Council (CSC), which is a non-profit institution with legal person status affiliated the Chinese Ministry of Education.

ISBN: 978-94-034-2373-9 (Printed book)

ISBN: 978-94-034-2372-2 (Ebook)

Cover design: Huala Wu & Bouwyn Stellingwerf

Layout design: Huala Wu & Claudia Tofan (Proefschrift Maken)

Printing: Proefschrift Maken, Utrecht

All rights reserved. © 2020, Huala Wu, Groningen, the Netherlands.

Cover and background images in each chapter are downloaded and modified from the website:

<http://616pic.com/>

university of
groningen

Pex3-mediated Peroxisomal Membrane Contact Sites in Yeast

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. C. Wijmenga
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on
Friday 21 February 2020 at 12:45 hours

by

Huala Wu

born on 2 January 1989
in Nei Mongol, China

Supervisors:

Prof. I.J. van der Klei

Prof. J.W. Veening

Assessment Committee:

Prof. A. Kortholt

Prof. D.J. Scheffers

Prof. R.J.A. Wanders

*To my dear Ama and ABa
my loved brother and his family
my loved sister and her family
For their love, support and careness*

致我敬爱的阿妈和阿爸

我亲爱的哥哥一家

我疼爱的妹妹一家

感谢他们的爱，支持和关心

A

Acknowledgements

Four years ago, I wished time would fly and let me accomplish my Ph.D. career as soon as possible. Yes, time never disappoints us. Now, I already spent more than four years in this lovely city, where I have met many wonderful people. I am very grateful to everyone who came into my life, supported me in different ways and walked with me throughout all this time. I also would like to acknowledge those who contributed to this thesis and supported me during my Ph.D. study. All experiences have become treasured memories forever.

First and foremost, I would like to give my deepest gratitude to my supervisor, Prof. Ida van der Klei, who gave me the opportunity to start my Ph.D. study in the Netherlands. I still remember the first meeting we had in your office. I was late because I got lost in the labyrinth of our unique green building. You allowed me to settle myself properly and then start my Ph.D. study. I learned a lot from the discussions with you in your office, where you always patiently explained the experimental ideas and mechanisms to me. I learned a lot from your broad knowledge, inspiring ideas and enthusiasm in scientific research. Many unforgettable moments stand out, such as the “brick theory” for writing an article or building up a research strategy, revising my conference PPT slide by slide and correcting my pronunciations of words now and then. But most impressive was guiding me out of my extremely stressful mind and teaching me that I should not place all of the burden on my shoulder at once. Also, I would like to thank you for your encouragement, which was very supportive during my entire Ph.D. life. All these experiences together with you have helped me to be a person with independent thought and an open, mature mind, which will benefit my future a lot.

Dear Arjen and Rinse, how lucky I am to have you as my colleagues. Without your help, I am not sure when I would have finished my Ph.D.. Dear Shifu (Arjen), you are not only a colleague but also a friend and sometimes like a big brother to me. Thank you for your patience all those times. I can't count the many times coming to you for all kinds of help through my entire Ph.D. career - countless disturbings. I guess my calls “Arjen, Arjen, Arjen or Shifu, Shifu, Shifu” will keep surrounding your ears for some time to come (Haha). Dear Rinse, honestly, I did not know how to approach you at the beginning because you seem very serious all the time. However, since we started to work together for some projects, I found you are very kind, smart and humorous. When I asked some questions or discussed some

experimental ideas with you, you always tried to guide me to find the answers myself or figure out whether those ideas are logical or not, which inspired me a lot. Arjen and Rinse, thank you very much for your priceless contributions to my thesis, your valuable comments and suggestions during the meetings.

Dear Jannet, how sweet and kind you are! Since I came here, you have been bothered by me a lot with all kinds of daily life things. Without you, my Ph.D. life would not have been that easy. You always comforted me and told me “no worries, I am here to help you” when I was in trouble with the invoice claims or extension application. “Dear Hualá, don't worry about your stay”, which felt like you removing the stone from my heart. I am grateful for what you did for me during my entire stay. Thank you very much.

My thanks also to my two nice paranymphs: Fei and Marc. Dear little fairy girl-shi mei, always energetic and positive, I was inspired by you so much (*_^). I am fortunate to have you as my shi mei. I never expected longevity noodles here on my birthday, and you cooking them for me was so sweet and such a big surprise. Then you kept preparing it for me for three years even when you were extremely busy with your experiments. Every spring festival, you always prepared gifts for me and visited me on new year's day. You are a sweet colleague, a pretty and lovely shimei and a close friend. All the best wishes to you, my dear xiao xian nv(小仙女). Dear Marc, first I would like to say thanks to you for being my paranymph. I wish I could be your colleague for longer. You are a very calm, humorous and sweet person. I hope you will have a lovely time in the Netherlands and you will always be very welcome to come to China for our delicious and spicy food.

Dear Renate, I am pleased to have you as my officemate. I noticed that you are critical in science and confident with everything. Your chocolate cakes are the best. I still have not tried the recipe that you shared with me. Maybe sometime you can be my bakery teacher. Good luck with your Ph.D. and I wish everything will go well. Dear Tjasa, you have a very positive attitude in life and always do your things with passion. The most important thing is that you are very enthusiastic and always nice to everyone. When we asked for your help, you would never say no. I wish you a fantastic Ph.D. life as well. Dear Asmaa, we always can meet each other on the way. All the best wishes to you.

I would also like to acknowledge those friendly people who already left our group. My dear lady (Srishti), many thanks for your support and company during my entire Ph.D. time. I am very appreciative of our countless times doing things

together. Our first trip made a big impression and we did masks on the bus, remember? We almost went to all the conferences together and spent delightful moments there. Thank you for organizing our group trip! Without you, I do not think we would have made it. That is one of my unforgettable trips and it let me get to know you guys more. Dear lady's husband-Sathish, I am happy you guys got married and thank you for preparing excellent food for us. I sincerely wish you and your wife have an extremely happy life and support each other forever. My dear ladygaga (Ritika) and dear wife (Justyna), our Hamburg time was full of fun. Ever since, we've had our private jokes about long or short noses. You guys are kind and sweet as well, sometimes like big sisters. Thank lady gaga for your patient explanations to my questions and thank you dear wife for teaching me that everyone should take care of their responsibilities. My dear Ann, you are so elegant, wise and sweet. You organized different activities to help us relax from our work and to have a lot of fun together. Ann's soulmate-Chirs, you are always there for Ann, which is so great. Your relationship is always sweet, which inspires me to imagine my future relationship. I sincerely wish you guys will have more and more wonderful life. Dear Natasha, you are like sunshine. I never see you are upset even though things were not going that good. I love your pizzas, which are the most delicious homemade pizzas ever. I will make a reservation for one pineapple pizza if some time I will go to Paris. Dear Arman and Terry, thank you a lot for taking me into the world of membrane contact sites. Special thanks to you, dear Arman. I learned a lot from you about the experimental skills and you are an excellent daily supervisor. I am sure you can be a very good teacher because you are patient with teaching and an intelligent person with critical thinking. All the best to you. Dear Terry, our group has had much happiness because of you. You are an easygoing officemate and I had a very happy time sharing the office with you. I got so many things from you when you and your wife moved back to China, which is so convenient for a new Ph.D. here. I wish your family will be always happy like the photos you posted on Wechat. Dear Chris and Kevin, you are very brilliant and well-organized with all your plans. Thank you for answering my questions and always giving me a lot of valuable suggestions. Dear Anita, you are a kind person at all times and very enthusiastic. I am happy to be your colleague and all the best to you.

I want to thank my other officemates for the lovely time: Corneliëke (my first master student, you are the best), Joana (always knowing exactly what you want), Tanja (lovely and nice girl), Harshitha (an enthusiastic girl all the time), Patrycja

(your cakes and snacks are so delicious), Kim (thank you for your lovely gift and I like your character), Robin (you are a very well-organized person and I enjoyed our chatting time even though sometimes I could not get your jokes) and Liam (my second and last master student, I know you will be a good student). Dear Marco, than you for inviting me to participate your lovely wedding ceremony. I wish you have a wonderful family and a very successful Ph.D. career. Dear Pragya, Thank you for organising a lovely girls' night. I also wish you everything will go well.

Please allow me to express my thanks to my Chinese friends using my mother language-Chinese. 民间艺术团的姐妹们，我来格村前一定是攒了很多人品，才让我遇到你们。汉堡包(陶叶晗)，我们的团魂，你可爱风趣的灵魂传给我点吧！心智比我成熟的你，总是能够醍醐灌顶，让我清醒。哈哈，我得记下来这件事：我真是怕你叫我大名，真是心头一紧啊，曾经的场景那是历历在目：你站在二楼“教育我”，然后气势汹汹下来继续“教育我”，我再也不敢发完消息就消失了。哥哥(倪海燕)，你有趣的灵魂也是戏精本精啦，和你的弟弟一起就是我们的团魂组合！佩服你身上那股科研劲儿，你不愿与人为争又超级让人信赖的性格，成为你的好朋友是我的荣幸。坚持你所认同的，不用太在意他人的评价，因为你是最棒的，表示也很想见见我们神秘的田姐夫(田杰)。小星星(王星)，我们永远的团长，领导气质，临危不惧的气场总是盘旋在你周围，和你出门可以完全不用带脑子，团长辛苦啦。可爱的招财猫气质也是无人能比的，以后一定请你来我家帮我招招财运。老王(王珏)，你是忍受我们叽叽喳喳最多的人，难为你了。很喜欢听你普及政治的知识，咋可以这么渊博呢！大美女玄仔(张文玄)，我们团的总体颜值靠你撑着了。我们的形象代言人，明明可以靠颜值吃饭的人，头脑还非常强大，时尚界和科研界你可以随时来回穿梭，表示我要抱紧大腿、不放手了。老张(张伟)，给人酷酷的感觉，轻易不说话，但说起话来那就是你的舞台，睿智的很。曾经还在团里的蒙哥(王蒙)，你真的是很讲义气的妹子，也很善良、体贴。还记得我们两还对爱情观进行过辩论，愿你找到心中所想的他。娇娇(张永娇)，没有到我们团发展，我们团损失了。钦佩你的精力、你的为人处事，喜欢和你谈天说地，更多地去交流内心的感受，能够成为你的朋友，开心！积极向上的心态，勇于走出舒适圈的勇敢 girl。罗马之行没有一起，希望有机会能够国内一起出游。姐妹们，超级感激你们对我的包容，关照，鼓励和支持，比心！让我们国内再聚齐。还有那些，希望有机会能够再走近些的美女朋友们：Keni(杨科妮，冻龄在18岁的小美女，羡慕)，宙宙(王宜宙，超级平易近人，性格也太好了吧)，娜娜(耿雅娜，每次见你都是文文静静的样子)，珊珊(宋珊珊，第一次你贤惠的形象和后来干练的样子都让人印象深刻)，杰琳师姐(张杰琳，专业能力好强哦，而且饱读诗书，和你交流真的是一种享受)和小娟师妹(也是很可爱的小仙女哟)。虽然我们相聚比较少，但坐到一起依然可以谈天说地，一起聊聊科研进展和不着边际的八卦。

据说我们 hoendiep 是中国城呢，也是再同意不过了。刚开始来的半年，我们基本上每周一聚，然后季师兄家就成了我们的聚餐根据地，甚至工作日下班后大家都会端着各自做好的的菜聚在一起吃，科研任务不重时的我们真是快活哟！

季师兄（季成涛），绝对靠谱、值得信赖的好朋友，印象中师兄还没对我们说过不呢。何维师兄，也是一位热心肠的师兄，我们聚餐的主力大厨。Hoendiep有你们两个师兄在，我们真是不怕蹭不到饭，有大厨和场地，生活很完美呀。闫师兄（闫星辰），很低调的学术达人，低调的为人下隐藏着幽默的灵魂。还有我们的大神（顾先明），博学幽默的你，对于各种话题都不在话下，厉害了。款姐（彭小红），小红，刀子嘴豆腐心说的就是你本人啦。知道你的人，懂你的善良、热心肠。你的独立也是成就了你的性格，你时刻武装着自己，让自己优秀，你做到了，棒棒哒！加油，我们未来的主治医师。小真真（秦语真）和杉杉（葛杉杉），有幸和你们成为好朋友，有好吃好玩的总能想起我，更重要的是你们会设身处地为我着想，给我各种建议，感激。美杉儿，我的形象顾问，以后很可能要跨洋指导我了，期待你们在美国的生活。昊姐姐（郭昊）和田宇师妹，聚餐的气氛一定要有昊姐姐，活跃气氛的能力我们都无法胜任呢。感谢美美的田宇师妹的盛情款待，你的笑很有感染力哦。海哥（付海根），双商都高的人，优秀如你，未来的学术骨干指日可待。许爸爸（许亮），稳重的爸爸形象深入人心，总是对未来有着长远的打算，一家人好幸福。丛师姐（丛郢颖），还记得你在季师兄家做的炸酱面，超级赞！葛大爷（葛洛），绝对的好邻居，超级感谢你的各种帮忙哦。姚鹏师弟，待客如此周到的师弟，真是不多见呢！谢谢每次的款待，愿师弟博士一切顺利。

还有中国城以外的小伙伴们，也是很多乐趣呢。苏和苏姐夫，文艺的苏，很喜欢你的画，也很赞叹你多姿多彩的生活，越来越同意，好朋友在一起，即使不用刻意去开始话题，待在一起就会很舒服。姐夫，乐观的内蒙汉子，感觉你总能笑对一切。祝你们的小宝宝健康快乐地成长。庆凯师兄（杨庆凯）和大萌萌（王萌），早点和你们认识该多好，可以早些多了一个吃美食、聊天南地北，谈心的地方。你们总是做好一桌好饭，备好一瓶好酒，等待我们大家的扫荡。回国一定还去蹭吃的。段丛，我们分享过很多小秘密哦，完全不介意我们继续探讨对未来家庭的想法。帅哥师兄（冯帅），真是被科研耽误了的吉他小能手，科研和演艺事业可以齐头并进呢。晓东师兄和宝杰师姐，谢谢你们在我焦头烂额时，给我定心丸般的开导。宝杰师姐，你喝醉的样子真的我见过最可爱的人了。邵闫和王总（王帆），幸运没有错过你们这对朋友。好喜欢你们两的相处方式和人生态度，积极向上，努力朝着自己的目标不停迈进。你们的爱情故事，可以找个编剧写成剧本啦，我一定拜读。晶晶师姐（邓晶晶），从来没有见过你丧着脸的样子，时刻爱笑的你，好运肯定都不愿与你错过！也感谢第一次去圣诞市场、不来梅之行的小伙伴们：华堂师兄（曹华堂）、媛媛小伙伴（王媛媛）和李静，多亏有你们让我加入你们，德国烤肠圣诞酒，问你快乐有没有。田蓓和水哥（郭淼），谢谢你们的盛情款待哦，我的格村写真怎么就泡汤了呢，蓓蓓，你快回来呀。小宇（张宏宇），我的网球好搭档，为师都不敢再喊你徒弟了，你的网球水平蹭蹭地提高了好多级，以后我要来取经了。大笨熊（陈倩），师妹呀，你怎么可以如此幽默呢，和你聚餐肚子会痛的。主播师妹（吴

颖颖），做美食总是很精致，具有一颗热爱生活的心，感谢会记得给我带国内的美食。小媛子（黎晓媛），每次和你聊天都会很舒服，赞叹你睿智的头脑和欣赏你洒脱的性格。

也要感谢曾经指导我的沈老师，谢谢您在生活上和科研上给予的帮助和支持。感谢我们敬爱的潘老师，你的一席话开导了我，让我下定决心出国深造。也感谢所有曾经在课题组给予我各种帮助的同门们，师兄（姐）们和师弟（妹）们，愿大家都越来越好。

感谢在我成长的路上所有关心我的亲人们，谢谢你们的关心和帮助。特别鸣谢我的二大伯一家人，你们对我的关怀，永记于心。也要感谢福成哥和嫂子，你们的援助之手温暖了我，谢谢你们。

最后也要感谢我的家人，你们永远支持着我，做我最坚强的后盾。阿妈，谢谢您，在您能力范围之内，您为我们已经做了很多很多，您无私的爱，是我们最温暖的港湾。我一直都很佩服您的坚强，和一颗永远向阳的心，您教会我们要独立、要善良、要积极向上。所以您要记得，您已经很棒了，永远不需要自责，更不要说您没有当一个好妈妈。阿爸，感激您和阿妈含辛茹苦抚养我们，支持着我们，您的恩情都在心里铭记着。哥和嫂子，你们总是会担心我在外面是不是没有照顾好自己，总是让我有事第一时间联系你们，习惯向爸妈报喜不报忧的我，在你们那儿我不管不顾，忧喜都要告诉你们。老妹儿和小宝，谢谢你们的支持，给你们也是添了不少麻烦呢。特别是老妹儿，似乎我们并没有真正异国过，四年来平均每天都在视频，甚至有时候各忙各的，有一搭没一搭说话，依然很暖，谢谢你的陪伴，让老姐没有孤单过。天天大侄子，大姑不希望你成绩一定名列前茅，更希望你每天能够开心快乐、做个阳光的小暖男。雯雯小美女，大姨好喜欢看穿美美的裙裙跳舞哦，还有你总要给大姨唱歌，暖暖的！甜甜小宝贝，大姨很快就要来看你啦，希望你这个国庆小宝宝茁壮快乐地成长哦！

In the end, I want to say thanks to my dear boy, Bouwyn. How we knew each other is called yuanfen (缘分) in Chinese and destiny in English. Thanks to your insistence, otherwise our relationship will not happen. Since being together with you, I grow up a lot but also become a happy little girl. We are always spoiling each other and let's keep doing it, agree?. My dear boy, you are wise, sweet and cute (maybe only in front of me). I also have the same feeling as you that you also have my back all the time. Thank you for your love, understanding, and support. Also, thank you for your professional designing guidance, comments, suggestions, and contributions to my thesis. Let's keep our 1+1>2 pattern and make efforts to achieve our same goal (^).*

Table of Contents

Chapter I	15
Peroxisome biogenesis and membrane contact sites in yeast and filamentous fungi	
Chapter II	35
Peroxisome development in yeast is associated with the formation of Pex3 dependent peroxisome-vacuole contact sites	
Chapter III	63
Novel peroxisome–vacuole contacts in yeast	
Chapter IV	71
Peroxisome retention involves Inp1 dependent peroxisome-plasma membrane contact sites in yeast	
Chapter V	95
Liquid chromatography–mass spectrometry identifies potential proteins of peroxisome-vacuole contact sites in <i>Hansenula polymorpha</i>	
Chapter VI	125
Conclusions and Outlook	