Compartmentalized signaling in the lung
Poppinga, Wilfred Jelco

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Acknowledgments
Acknowledgement

A man’s friendships are one of the best measures of his worth

Charles Darwin

Looking back from this moment to February 2010, when I would start my final internship and first touch upon AKAPs, many lives have touched mine and one cannot help but be influenced by each of those interactions. Science is a wonderful world to meet many people from all around the world; however it would also sadden me to see so many people leave my life again. It would be too much to mention every single person that has crossed my path in this long period, so let me begin to say that I acknowledge every person for their contribution to becoming the person that I am today and hope to be forgiven if your name is not mentioned individually.

Let me start at the beginning with the lab in Berlin, Enno Klußmann, you were a patient person allowing me to explore all that I wished to study. Thank you for providing me an opportunity to start something that I could not have done in the Netherlands. Philipp Skroblin, you helped me practically with starting up and would remain a source of information even after leaving back to Groningen, together with Antje you also showed me the Berlin nightlife. Antje Schmidt, also thank you for helping me to go to a dentist when I really needed some German assistance, it was a life saver.

Kerstin Zühlke and Jens Furkert thank you for helping me with the more radioactive experiments and also for assisting my student Laura when she joined your lab. Andrea Geelhaar and Beate Eismann, two wonderful technicians, we would communicate using both my limited German and your English and everything in between, but we could always manage and you were always prepared to help. Danke Schön!

Dörte Faust and definitely also Matthias Pfeifer (Horst), you remained my best connection after leaving Berlin, always allowing me to stay at your house to visit thesis defenses and later when you moved to London to stay and visit during my meetings and courses there. I am sure we will stay in touch and find out way in or
outside the scientific world. Berlin has given me good friends and hopefully longtime collaborators.

In Groningen I would like to thank Martina Schmidt and Harm Maarsingh for providing me the opportunity to turn my work from Berlin into a grant proposal, allowing me to follow my own ideas. Having received several offers for projects already funded at other departments, I should thank Herman Meurs for convincing me to stay when there was no money, stating it was a unique opportunity to create a new research line. Something that would eventually prove to be true and lead to many other PhD’s joining my quest for compartmentalization in the lung. Nothing more thrilling in science than to see your ideas grow and blossom.

Irene Heijink thank you for support during my PhD, but also for believing in my ideas for a grant to start with my post-doctoral career. But also to provide support when I would feel that my own department would fail to provide this.

This is perhaps also a good moment to acknowledge my reading committee, thank you all for reading and approving my thesis. Uli Eisel, together with Ingrid Nijholt you brought AKAPs into the context of Epac compartmentalization and my Master project was originally aimed to copy this into the lung, without you this thesis would not have even existed. Sven van IJzendoorn, we mainly interacted when I would use your microscope in the early years of my PhD, you published on AKAPs one year before Uli making you the original Groningen AKAP expert. However Groningen has not been able to keep its interest in AKAPs, I hope this will now change. Ray Penn, we have met each other on several occasions, either when you would visit our lab for a thesis defense or at the ATS or YIM. I am happy you agreed to be on the reading committee. As most people that I met that worked on AKAPs before, you also did not seem to enjoy it very much. However being the only one besides me that worked on AKAPs in airway smooth muscle you would have to deal with my excitement about this topic. Thank you for bringing in sometimes heavily required advice, talking to you has shaped several chapters in this thesis.

With an increasing amount of people working on compartmentalization, I should thank those people in particular for a great collaboration, sharing our growing pains in science. Anouk Oldenburger, thank you for teaching me my first human cell culturing techniques after working only mainly with bacteria and fungi. You have been able to start with AKAPs in the epithelial barrier, which was eventually published quite nicely, providing a lot of work for people in the future. Sepp Jansen looking from the cancer perspective also trusted in my suggestion to look for a role of Ezrin in epithelial-to-
mesenchymal transition which was also appreciated by the reviewers, and this was published quickly. Thank you our interesting talks.

**Pablo Muñoz-Llanca**, always critical on AKAPs, as I was on Epac, you and I were able to write a nice review summarizing quite nicely what I would expect to be the role of AKAPs in β₂-adrenoceptor cycling. Knowing now more, one might wonder how much is true, but it was a great start for a hypothesis. Of course Pablo, you were more than just a co-author, I had the “pleasure” and honor of being your paranymph, standing by to support you during your defense and everything leading up to that moment. You and I had drinks, too many to mention, leading to the best discussions on scientific topics. I am sure when you come to your senses and focus again on some AKAPs we can have many nice topics together to study in the brain. Now we both have become lone wolves again, but we shan’t forget the wolf pack.

**Bing Han**, you were my asthmatic counterpart; starting on the original ‘good’/‘bad’ AKAP hypothesis in asthma. Although this did not go as expected and you were diverted more to company projects, leading to a nice publication on Sul-121, we also finished a project together to be published in your thesis and hopefully a paper or two. Now you will continue as department head for animal studies at Mucosis B.V., I wish you luck but I am sure you will do fine! Thank you for your teachings on China and being a support when both had to struggle to get our thesis to the reading committee.

**Haoxiao Zuo**, coming to the department as Bing’s girlfriend, later fiancée and eventually wife, you became my student upon my request as I saw that you could do much more than was provided to you at the time. You set a foundation for AKAPs in EMT and on my recommendation you later became a PhD focusing on cAMP/cGMP compartmentalization using FRET reporter mice. Thank you for still including me in the discussions, I still believe in the idea and I hope you can achieve our goals in this project. I will stay in touch to help you, as I know you and I both appreciate the discussion.

Not only PhD students provided support, also **Carolina Elzinga** was a major support for me inside the lab, but also inside my mind when things got tough. Always available even when not in the department, you tried to always help me understand why people act in certain ways or explained to me to just accept things as some people will never change. To you perhaps the quote at the beginning of my thesis should make the most sense. Reminding me that happiness should be a priority and that a PhD is not a necessity for that happiness, gave me inspiration to keep on struggling, as you told me many others had done before me. Only the faces change, not the problems.
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Also the other technicians gave support and sometimes much needed comic relief, especially Mark Menzen who was one of the few that made me feel welcome from the start. You found a better future before I left, leaving too soon, however I wish you much happiness with your newborn family. Sophie Bos and Annet Zuidhof, I appreciated your company and especially that you helped me with killing the animals and/or counting endless slides with cells, I would not have been able to do it alone, thank you.

I would also like to thank the many students that I have supervised over the last years, especially the students that have stayed for several months. It was always sad to see you leave.

Adinda Mieras, you helped me to set-up AKAPs in the brain, although this never really continued, I enjoyed learning together about this, you were very eager to learn and went above and beyond to prove your worth. Years later you have started your own PhD studies and I wish you good luck with that.

Laura Holtzer, you went to Berlin for me, back to where I began. You continued characterizing the AKAPs expressed in the airway smooth muscle cells and helped me tremendously with your western blotting skills. I think you were a very smart student and I feel you would have made a great scientist. You preferred to continue as a pharmacist; however not without leaving with a co-authorship also found in this thesis as chapter 3.

Sjoerd de Haan, you always talked too much and you have made it into your career, as an account manager. I think you have found your calling. A lot of your time was spent talking in the coffee room or in someone’s office, but you worked hard and I enjoyed having you around and I hope you can still use some of my teachings in your future career.

Saskia Driessen, you were a very hard worker. Not really used to socializing with your supervisor, you preferred to refill pipette tips and clean the lab. I think every student can learn from you. Luckily you loosened up and I think we had a great time. I hope you enjoyed, even when everybody was focusing on your face turning very bright red, you still could stay professional. Another student lost to the pharmacy, but I hope you enjoy it.

Ksenia Myacheva, the red threat from Russia. I had the weirdest conversations with you I have to say. I really enjoyed having you in the lab, bribing me with Russian money which was quite worthless to you, but precious to me. You did great work and together with the work of Haoxiao, I think we made a very nice EMT story,
although we will have to wait whether this will still be picked up for publication during Haoxiao’s PhD studies. As a TOP master student, of course you continued to do a PhD at a top institute. I hope to hear more about your science soon.

**Sybring de Vries**! Very quiet girl, but secretly having a great sense of humor and really talkative if someone could finally pull it out of you. You were amazing with your pipetting patience, dozens and dozens of 48-wells plates you pipetted for genetic characterization of the AKAP12 mice. Dozens more pictures you took and quantified for histological characterization of the AKAP12 mice. I am happy to say that not all went to waste and you came to be co-author of chapter 4. Sadly we never got the time to do the same for the AKAP5 mice. Although you were promised a job at our department, money never came, but now you luckily have a job as a technician in the best province the Netherlands has to offer.

Of course there have been plenty more students staying for only a few weeks and **many more students** supervised by others that I have shared great moments with, thank you all for your company and fun moments.

To close on my direct collaborators, I want to acknowledge all of my co-authors not already mentioned. **Christian Gonzalez-Billault**, we have worked together on our review, which I feel is a good start of my book. I hope in the future we can collaborate more on studying compartmentalization in neuronal systems, I think there is still more to explore. **Andrew Halayko**, you always had good comments on my papers when we used the hTERT ASM cell lines. You have a great sense of humor, pleasure to meet you around ATS, YIM and other meetings. If I ever have the urge to work with hTERTs again, I will know where to find you. **Irwin Gelman**, we have only had contact via the e-mail and yet I am thrilled to have an expert on AKAP12 be a co-author on my papers, thank you for letting me use your AKAP12 knock out mice, it allowed us to test our **in vitro** work in a system more closely resembling the real situation. **Wim Timens** as a pathologist you taught me to recognize the airway smooth muscle bundles in histological stainings and you always had great suggestions to improve the paper and the statistics. Thank you. **Laura Hesse**, without hesitation you helped me to get data on KC release in my mouse samples. This to me shows the real power of GRIAC, especially as you expected nothing in return. Of course, I was very happy to acknowledge you with a co-authorship. Thank you very much! **Alen Faiz**, thank you for your help with the eQTL analysis and your large amount of patience, trying to explain to me what you actually did. I am really happy to have a paper that can put this thesis closer to the patient situation. **Maarten van den Berge**, also you helped to arrange a lot of things with the eQTL
analysis and to arrange things with the eQTL lung consortium, thank you also for looking
to the manuscript in detail and trying to teach me how to write this properly. **Judith Vonk**, you performed all the SNP analyses regarding the association with the improvement of lung function and the link with smoking. I could not have understood how to write this paper without you and you have taught me some of the different languages epidemiologists speak compared to my molecular biologist language. Thank you. **Corry-Anke Brandsma**, although our interaction was limited for this thesis, we have interacted on other occasions, especially as you brought some more AKAPs in the lung field. To you they might just be genes, but I will be curious to see what happens with Ezrin and MAP2, as Ezrin is next to AKAP12 one of my favorites. Similar for you **Gerard Koppelman**, you brought me to AKAP1 and perhaps I can study more on the role of this AKAP in lung diseases in the future. Time will tell. Thank you all.

Of course, there are many more people within GRIAC to thank and I would especially thank **Dirkje Postma** to be willing to give me some guidance for my future and tell me to talk to Gerard about AKAP1, it helped me to move forward in my career. Seeing your farewell symposium also inspired me to find a great mentor and hope to be a great mentor to others in the future.

Working in a department, one interacts with a lot of people not directly involved in your work or even in similar topics. I would like to thank all those that have assisted me in the year whenever I had questions or trouble or just to have a drink with.

Allereerst een belangrijk persoon die niet echt onderdeel is van de afdeling, speciaal voor jou in het Nederlands, want Engels is niet je favoriete taal. **Sylvia van der Heide**, je bent meestal de eerste person die mij begroet in de ochtend en je hebt (bijna) nooit geklaagd over de rommel in mijn kantoor of de blikjes bier in mijn vuilnisbak van de avond daar voor. Je bent de enige geweest die mij ooit heeft kunnen dwingen mijn bureau soms op te ruimen, zodat jij je werk kon doen. Dank je wel voor de leuke tijd en ik hoop je nog eens tegen te komen!

An important drinking buddy was **David Wright**, the first “real” post-doc I could experience in the lab, leaving so very quickly again to start a new career in scientific communication. We will keep in touch through the wonders of the internet and I hope you will find a good career outside of academic research. **Tim Koopmans**, of course you belong to this same category, eventually only lone wolves will remain, but we will keep in touch. We shared the burden of being Pablo’s paranymph, thank you for letting me annoy you in your office when I needed to. Also a thank you to **Hana Černecká** for your friendship and giving me the honor to be your paranymph, it was nice that you
joined me to study for the diploma in advanced pharmacology. As a lab head you are already becoming an important person at Bayer and I am sure that your career will proceed very rapidly. Tjitske Oenema together we were Hana’s paranymphs and you were always the source of information for me within the department, staying up to date with all the social developments. Now you are study director at ABL, another former colleague with a fancy sounding job, you deserve it and I hope you enjoy it. Kuldeep Kumawat, the hardworking Indian, perhaps my favorite office mate during my PhD, you always showed to be the most informed on the scientific developments in our field; one of the smartest people I met in the department. Although you went for the US, you came back to the Netherlands again now Post-doc in Utrecht and hopefully soon able to start your own lab somewhere. Pavan Prabha, our time together was short, your sense of humor is weird but you were fun company we shall have a beer in the future. Good luck with all your research aspirations, curing the problem of air pollution. Boy van Basten, also our time together in the office was short-lived, although you are one of the people in the department I knew the longest, starting already at the student dancing society SSV The Blue toes and you did your Bachelor and Master projects with Anouk. I enjoyed our conversations; we were very different, although somewhat similar in other aspects, besides the dancing and watching dr. Who, we also had a unique way of looking at the world and its inhabitants. You continued to work more in the education part with Martina, but now you have managed to start a PhD in Scotland, I wish you the best of luck and hope to see your papers soon.

Now remains some seniors of the department. Reinoud Gosens, we had great conversations during drinks, meals and conferences. Having experienced you for more than six years, now an associate professor, I think you will continue to progress through your career rapidly and I am sure that I will contact you in the future for advice on career progression in (pulmonary) science or to take a glance at my grant proposals. Thank you also for suggesting me to discuss with Gerard on AKAP1, although the direction changed, it was the hint that would lead to my next job.

Hans Zaagsma, always willing to talk about science, to provide guidance and curious about the progress of the “Akappen”, you are an example of the truly passionate scientist and I wish to be able to keep the same passion for as long as you have. Thank you for allowing me access to your knowledge and advise me on my career even more than 10 years after your retirement from our department.

Jacques Hille, we shared an office in the final months of my stay at the department. However, we were already in touch from the start when you allowed my
students to use your office space to write their report and process data. We had nice
conversations and you could provide me insights from a different perspective. I valued
our conversations and I hope you enjoyed them as well.

Spending months at a department I had done several times before. However,
years were a new experience and it was one that I was not really looking forward to, as I
worried to get bored. However, it became clear quite quickly that the only way I could
continue studying AKAPs was to get a PhD. Since then many, many people not yet
mentioned have passed through the department or are still there that have influenced
this long time spent at the department. I hate listing names, therefore I thank all the
other (former) members of Molecular Pharmacology that have not been mentioned
yet for the lessons they had to offer me.

The final groups of people that I got in touch with during my PhD are those that
provided advice and/or service to allow proper experiments to be performed. I would like
to thank Ben Giepmans and Klaas Sjollema for all their help with my cloning of the
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hope that someone will continue with this work someday. Marjan Luinge, my go-to
person in the Pathology lab, thank you for aiding me in my staining protocols which
could not be done in our lab. Roelof Jan van der Lei, you were essential for my FACS
experiments to purify my EosFP-expressing cells. I am happy we got to work together at
least briefly so many years after our time studying in Leeuwarden. Finally, for all my
animal chapters I depended a lot on the CDP to assist me with the breeding. Thank you
Yvonne Hedema and Pieter Steijvers, for keeping my mice alive and Juul Baller to
help me set up the breeding lines.

An important part of the thesis occurs outside of the lab, where ideas can hit
you unexpectedly. For me this was especially true while deep under water during my
SCUBA diving with GBD Calamari and Duikvereniging Hydrofiel; for which I would like
to thank all the members together as there are too many to mention separately.

Of course, my number one diving buddy should be mentioned separately as a
friend from high school, colleague at IMENz, diving buddy since 2011 and my
paranymph, Robert Woudstra. Together we learned how to dive during our stay on
Gran Canaria and we have been able to log many dives together in the Netherlands and
in the Mediterranean Sea. We have followed similar pathways coming together again as
technicians in the same company and sharing our networks in Groningen. I hope to log
dives together again in the future!
I am happy that I have been able to stay in touch with good friends since high school, David de Groot, it was a different millennium when we first met and yet, Pokémon have returned again while writing this acknowledgement. Many things have changed, and yet so many things have remained the same. We were the only ones going to the same applied university after high school and we have had a nice time also partying in Groningen. Peter van de Lageweg, starting also in Leeuwarden after high school, you and I were not satisfied and both continued for a Master’s degree. However, you went very far away from Frisia, all the way to Eindhoven, but you always wanted something better than Frisia. Now you are a graduated architect working in Amsterdam on apps for construction sites. Another interesting addition to birthday parties is Ynze Goinga, now studying in the UK and I think I should call you a civil engineer, although the civil part… Together with Peter you are the real engineers in the group and I expect great things when you will graduate. Lars van Dorenmalen, the international businessman, I have missed you at too many birthdays and I don’t really understand what you do, but you are for sure one of the people interested in the world and its wellbeing, volunteering at the moment of writing in Bangladesh to increase sustainability. I am happy to count someone this responsible for our future as one of my friends. Marleen Lamberts, the only girl from our little high school group. The first to have a child, Ayden Lamberts, a wonderful young man that has a great group of guys to look up to. You have always been a great friend, someone to talk to and have deep thoughts with. I am sure it has sometimes been hard to be the only girl, but growing up with brothers allowed you to handle us appropriately. We have all come a long way since our times at the Drachtster Lyceum, relationships have come and gone but I am happy that have been able to stay connected. I am sure that our friendship of so many years will continue no matter the distance.

Valerie Wiersma, you were there in high school, during my Bachelor, Master and you are the only one that continued with me into a PhD. Our paths have been so similar for the last 15 years or so and you eventually even married into GRIAC with Daan Pouwels. Your passion lies in your family, which should be expanding around the time of my defense(!), but I am sure that your intellect and talents will not be lost to science and you can continue your career as a power couple with Daan as the future of the lung field and you the future of the cancer field. Both of us suck at keeping close when focusing on our research, hopefully we can now start again after getting rid of these PhD studies. Perhaps we can have future collaborations, AKAPs are of course important in cancer as well (also in DAMP signaling).
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Speaking of being bad at keeping in touch, other friends from my Bachelor studies must have felt neglected for the last years also and I hope to make up for this one day. The brothers Meihuizen, Gerard Meihuizen you have become a farmer and a father, big changes since our time in biotechnology. Rolf Meihuizen, the best of us, always keeping in touch and showing your social skills, now finishing your second study at the University of Utrecht. Hope you can find a fitting career after this. It is fitting that perhaps my only true Groninger friends were studying in Frisia and you prepared me well for my time in Groningen. Brandt Meylis, actually one of the few people from Leeuwarden that I know that actually ended up doing what we were trained to do. You had to go all the way to Leiden to do this, creating difficulties to meet each other too often, but I enjoyed Leiden the few times I was there and you convince me that it might be a nice city to work. Years have passed since our times in Brandt’s hokje, complaining about certain teachers whose names shall never be mentioned again. It is perhaps true that the best friends are shaped in shared misery. There were of course others that shaped my time in Leeuwarden and during the 1.5 years spend on internships in Groningen thank you all for the memories and lessons that formed the mind and the person capable of doing this research. Thank you all.

My oldest friend, Sijtze Henk Wiegersma, it has been since the early ‘90s that we have been friends spending our holidays playing games, learning all about Grand Theft Auto without the help of the internet. You stayed with the cars, as you have always wanted to be a car mechanic. We have always been able to talk about anything and find support. You have shown more wisdom to me than some people carrying a PhD, never be limited by the opinion of others. I am sure you can do whatever you put your mind to, every education was a battle that you have won. I am proud to call you my paranymph.

Staying in Boornbergum we get to family, without the mental support of family I would never have been able to become the first member of the family to go the university and even get a PhD. Avelien and Marijke Huitema, always mentioned together in my memories, twin ladies with such different personalities. We grew up together in the same street, eventhought you were my cousins you have always felt like sisters to me and I was honored that you could be my witnesses at my wedding. Avelien, you have shown that struggle will be rewarded and I hope you can start soon as a teacher or as anything you can really enjoy doing, you deserve it. Marijke, together with your now husband, Nicola, you have left Frisia far behind to go to Belgium to be able to stay together. Nicola Williams, you left everything behind in Africa for a better future. Together you have taught me to leave the comfort zone to improve your situation.
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Alexander Poppinga and Anje Geerligs, you have provided me the honor of being an uncle to Jurryt and Thymen who will continue our family name to the next generation. Thank you for being part of the family. Heit and Mem, you provided a crucial ingredient to this thesis, the name on the cover and the person behind it. Growing up in a family of entrepreneurs I learned that work does not stop on Friday or after five o’clock, if you want your company to succeed it needs to be a part of you and you need to be a part of it. A company, a career, can only be as succesfull as the amount of energy you put into it and expecting things to be arranged for you and handed to you will lead you to fail when the people supporting you leave your life. Thank you for many life lessons that have shaped me.

Moving far away to Indonesia to save perhaps the best for last. Putri Wulandari, without a doubt a creative brain to support me with obtaining the final form of my thesis. Many thanks for your creative input and hard work on that and also for taking care of Vessa for me while you are staying in the Netherlands. To us, you are part of our Indonesian family.

Herren Tania, being my brother (in law) now officially, you have entertained me with a good supply of games while in Indonesia and you have enjoyed our house in the Netherlands, perhaps inspiring you to move your newly founded banana business to Europe? Being the youngest is never easy, I know, but you have the opportunity to learn from your older siblings that have graduated before you. I hope we can continue to support your growth and you can perhaps make the whole family rich soon. Hanel Tania, together with Herren you are the younger siblings I never had, the benefits of marriage. You have started your own marriage recently with Sylvia Gunawan and will explore all that comes with marrying a woman with a PhD. I wish you both a lot of happiness in this new adventure. You are the business power couple of the family, together with Herren you are sure to hear from me, when academia will leave me poor in the streets!

Gotok Hianwijaya and Aprillia Linggaraja, thank you for being such caring parents for Vessa and supporting our relationship with such enthusiasm. I am sure many can only wish to have such a close family connection spreading over the world.

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Chapter 9

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