

Cancer, Stem cells & Developmental Biology

Newsletter June 2017



Introduction

Dear CSDB'er,

Cheers to you! You survived the Dutch rainy depressing winter and the academic year is coming to an end. Finally, you can enjoy summertime! Too bad you are still in the lab working your asses off...

Luckily, the StuCom is organizing a BBQ next week, so we can have a break of the lab and drink a few (or more) beers, have a nice dinner and enjoy the sun. If you haven't signed up yet, don't forget to send an email to **stucomcsd@gmail.com**.

Unfortunately, this will be the final activity of this academic year already, but don't worry: in September a new StuCom is taking over to provide you with awesome 'borrels', fun activities and seminars and to top it all off a retreat to another awesome location. What fun we had this year in Bonn and Cologne! We really enjoyed organizing it for you, but thanks to your enthusiasm and 'gezelligheid' the retreat was a great success. Thank you for that! You can find pictures of the retreat and read all about it in the next newsletter, which will come out in a month or two. In the meantime: don't forget to upload your photo's on the drive, so we can include and share them.

Since a few months have passed since the last Newsletter came out, let's freshen up your memory... We had the seminars of Frank Bos and Jarno Drost, which taught us a lot about imaging and organoids. Afterwards we had some beers and not be forgotten: ate a lot of pizza! Besides seminars, we also had a fun pooling activity in Cafe 't Hart.

In addition to the seminars and the fun activity you can read in this newsletter about the second internship experiences from Eline, Gaby and Jet in Switzerland, Sweden and England. Especially for those of you who are still in doubt of what place to do their second internship it can be helpful. Finally, you can find a wall of fame in this and coming newsletters. If you feel like it, please send in your most beautiful or funny result and claim a spot at the wall!

See you at the BBQ and for now: enjoy reading!

Warm regards,
Femke

Content

Introduction	2
Seminar Frank Bos	4
Student Abroad	6
Pool Event	11
Seminar Jarno Drost	12
StuComics	14
Colofon	15



Seminar

Frank Bos



On February the 5th, we had our second StuCom seminar. Honours were to Frank Bos, Postdoc in the Van Rheenen group at the Hubrecht Institute, who gave us an interesting lecture about techniques used to visualize developmental biology. During his PhD in San Francisco, he worked on visualizing hematopoiesis in embryonic development.

For this project, he used several zebrafish models. Zebrafish are of great use when studying hematopoiesis

as they allow for easy visualization of the hematopoietic processes. He used zebrafish to find genes involved in angiogenesis. After randomly mutating this model organism, they discovered a mutation in CCBE1 that results in a lack of lymphatic vessels in both zebrafish. In addition, CCBE1 mutations in humans lead to Hennekam Syndrome which is characterized by an abnormal lymphatic system. After an interesting introduction on Zebrafish angiogenesis and vasculogenesis, the term Intravital Microscopy (IVM) was introduced.

IVM, a technique the van Rheenen group is now famous for, can be used in several scientific approaches. Regarding angiogenesis, the technique was used to visualize the sprouting of lymph vessels from venous endothelium along the arterial vasculature. Even in the broader field of hematopoiesis, IVM has proven to be of great use. After optimizing the protocols, IVM was used to allow long-term (<2 hrs) imaging of extra-embryonic development. This led to the discovery of circulating hematopoietic cells. Tracing back these circulating hematopoietic cells and making use of stem cell specific markers, the combination of these techniques made it possible to find the origin of the Hematopoietic Stem Cells in the aorta of the developing embryo.

Currently, Frank Bos is optimizing his protocol for visualizing extra-embryonic development using IVM. He tackles several hurdles such as keeping the embryos alive outside the mother's womb, while still providing sufficient conditions for the embryonic development to continue. Frank now focuses on the development of the skin and mammary glands using Lgr6-expression and markers for EMT and MET.



Student Abroad

Eline Brombacher - Zurich

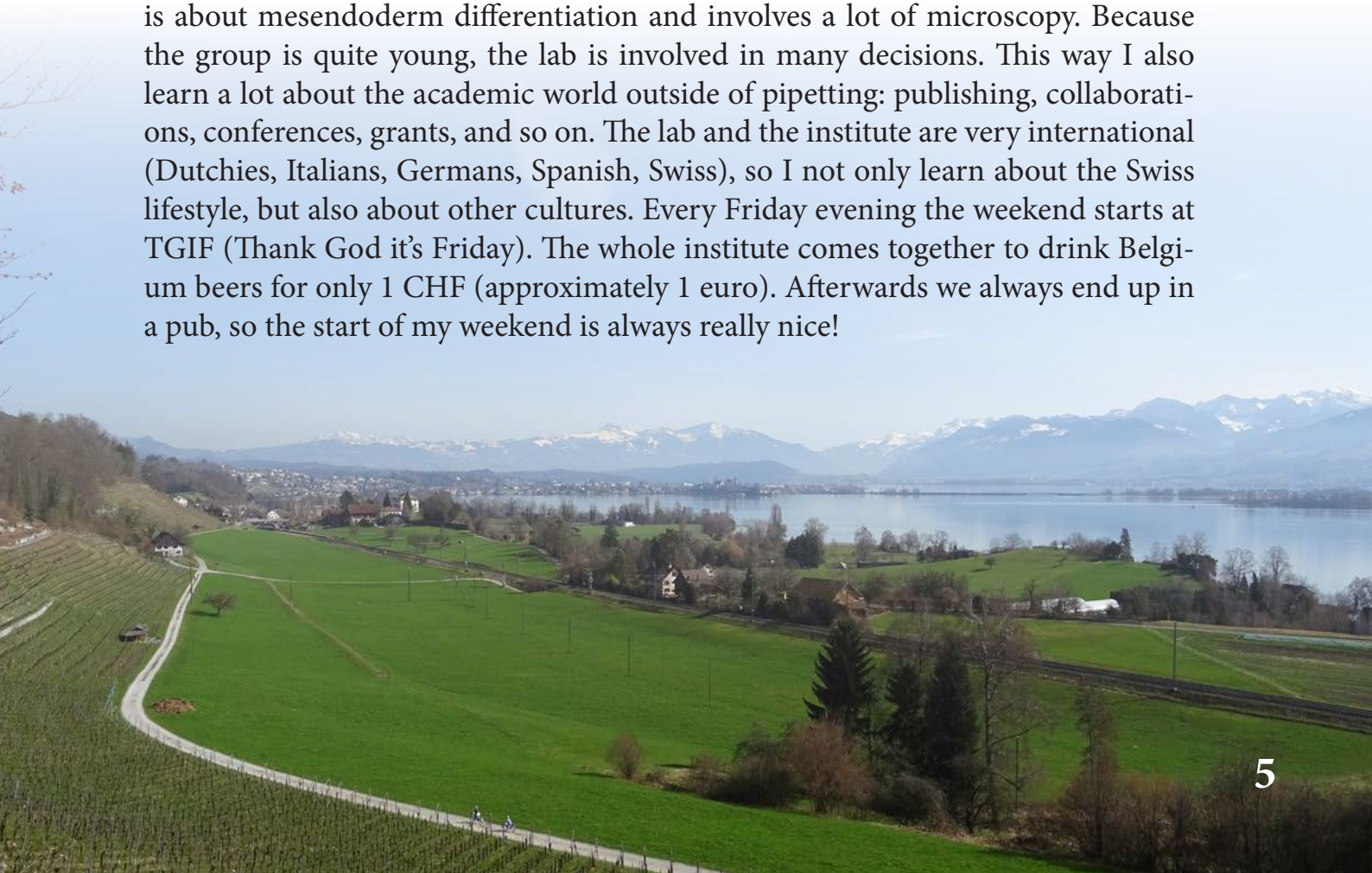
Hi everyone,

Or as the Swiss would say: grüezi mitenand. In January I started my internship in Zurich and I'm happy to share my experiences with you.

As long as I can remember my parents took me on holidays to Switzerland. I fell in love with the mountains and therefore it was quite easy for me to pick a country for my minor internship. The other thing I knew was that I wanted something with developmental biology. A colleague at my first internship had a friend in Zurich, who worked with zebrafish. She is now my supervisor. So finding a lab was not too hard for me, but the paperwork that followed took quite a while.



I'm doing a six month internship in the lab of prof. Mosimann. He is an expert in cardiovascular zebrafish development and CRISPR/Cas9 mutagenesis. My project is about mesendoderm differentiation and involves a lot of microscopy. Because the group is quite young, the lab is involved in many decisions. This way I also learn a lot about the academic world outside of pipetting: publishing, collaborations, conferences, grants, and so on. The lab and the institute are very international (Dutchies, Italians, Germans, Spanish, Swiss), so I not only learn about the Swiss lifestyle, but also about other cultures. Every Friday evening the weekend starts at TGIF (Thank God it's Friday). The whole institute comes together to drink Belgium beers for only 1 CHF (approximately 1 euro). Afterwards we always end up in a pub, so the start of my weekend is always really nice!



Not only the beginning of my weekend is great, every weekend feels like a holiday. It's absolutely amazing to live between the mountains. In winter I went skiing almost every other week and I'm currently wearing my hiking boots every weekend. If I'm not in the mountains there is always something to do in Zurich. A bike festival, free wine tasting at vineyards and music and dance festivals are some examples. Another advantage of living in Switzerland is the central location. Many other European countries are easily accessible. During easter, for example, I've been on a road trip to the north of Italy, only a 3 hours drive!

The big downside of Switzerland is of course the costs. Almost everything is 2-3 times more expensive compared to the Netherlands. Also the salaries are really high, but as a student I can't benefit from that.

In my opinion Switzerland is a great place to live. I'm currently looking for a job and I hope that I can stay in Switzerland for another year or two. Please let me know if you have any questions about this country or an internship abroad, I'm happy to help!

Ciao mitenand!

Eline Brombacher



Student Abroad

Gabriella Darmasaputra - Stockholm

I arrived in Stockholm in November 2016; which I realise now was not the brightest idea (pun intended). November in Stockholm is the beginning of the long dark winter, and we also had the snowiest November day in 111 years last year. Talk about a warm welcome.



To tell the story properly I have to start in the beginning. I started looking for a group to perform my minor internship in the spring of 2016. I wanted to stay in the field of hypoxia and cancer metastasis and work with new techniques. I was interested (and nervous) in working with mouse models and immunology. With the help of my previous supervisor, I contacted a couple of labs in the UK and Sweden and got into contact with the group of Prof. Randall Johnson in Karolinska Institutet.

Prof. Johnson is well known for their work with hypoxia and the HIF proteins, and next to this satellite group in Stockholm he also manages a (larger) research group in Cambridge. Since I arrived, the interactions I have with my colleagues have been very helpful with understanding the Swedish culture and values. During fika (coffee and pastry time), we would discuss everything from experimental setups to the state of politics (a crowd favourite) and even memes. Even though I expected Sweden to be very similar to The Netherlands, it certainly has its own quirks. Two examples is that the Swedes are cautious and communicates in a less direct way, and the very prudish way they deal with alcohol sales. This regulated alcohol sales certainly increased the importance of boat trips across the Baltic Sea, where alcoholic drinks are sold tax-free, for students. I have also taken part in this infamous 'booze cruise', and I can certainly recommend it at least for the entertainment values of watching a drunk Scandinavian/Eastern European dance floor.



During my time here I have experienced the ups and downs of being an international exchange student; the excitement of visiting and experiencing as many places as possible, the feeling of loneliness when your new international friends leave the country, and the thrill of new friendship. I learned that people in Stockholm love to dress almost exclusively in black, to eat out both for lunch and dinner (better book that table), to exercise out in the cold, and to swarm outside scantily dressed with the slightest hint of sun. I am also proud to say I now possess the skills to walk on solid, slippery ice in subzero temperatures without breaking any bones.

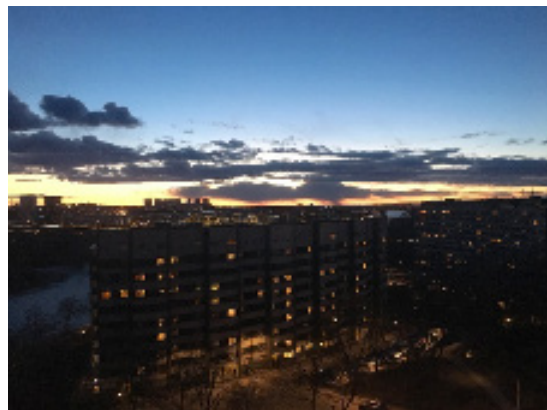
My current project involves working with mouse models. I found out how the workflow of in vivo research is different from in vitro research. Experiments have to be very well planned to make sure that as much data can be retrieved from one animal experiment. One other thing about animal research is the waiting period to get the right mouse to be bred. However, since waiting for the mouse pairs to get it on is not a legitimate research method, I also learned to plan well and fill my days efficiently (like by writing this story).

On that note, I will end my story here and continue thinking about the fact that mice have the tiniest, cutest tongues that they use to lick water from their drinking bottles.

Hej då,

Gaby

PS. If you are interested in an internship in Prof. Johnson's lab, you can drop an email to **Helene.Rundqvist@ki.se**.



View of Stockholm from my housing



Wednesday night drinks with housemates



When the water freezes, all the ice skates come out

Student Abroad

Jet Segeren - London

Writing about my internship reminds me of one of the most exciting periods in my life. I really wanted to perform my second internship abroad as it is an easy opportunity to live in a new place and get to know a complete different environment. I had mainly two requirements: don't be very far from The Netherlands and to improve my English. Therefore, the U.K seemed to be a perfect choice for me. After sending out a few emails, I had a Skype call with the famous kinase scientist Peter Parker. Finally, they were very happy to host me in their laboratory and gave me the opportunity to perform my research project about the therapeutic potential of the G2 catenation checkpoint.



On a rainy day (no the first one, neither the last one...) in October 2015 I arrived to what was going to be my home town for the coming 8 months, London! Cool place! As real Dutch girl, I joined a hockey club and bought a bike. Cycling in London was not as easy as in Utrecht and turned out to be sometimes quite dangerous. However, it allowed me to get to know the city faster and in a Dutch way.



After a few days of sightseeing it was time to start my internship! The Francis Crick Institute is the biggest biomedical research facility in Europe. I really felt that I was in a cool environment with ambitious multicultural researchers that everyday try to do their best to understand diseases and working on finding new treatments. I spent most of my time in the high throughput and microscopy facility trying to understand the different behavior of lung cancer cell lines in response to catenation stress. Based on a previous finding in the lab, I tested the potential of inducing severe catenation stress in these cells to trigger cell death.

Besides learning a lot about cancer cell biology, my colleagues very well introduced me into the English pubs. I became a big fan of diffrent beers and got to know my colleagues and the British cult re very well. Although weekdays were hard-working, I had enough time to explore London and surroundings. Som times it was great to leave the big city, rent a car and explore small villages around London. The driving part was always a challenge but ... I managed to survive. However, most of the weekends I enjoyed the big city with all kind of festivities throughout the year. Of course I also missed friends and family sometimes, but it was really worth it. If you have the opportunity I would definitely recommend you to go abroad for one of your internships!

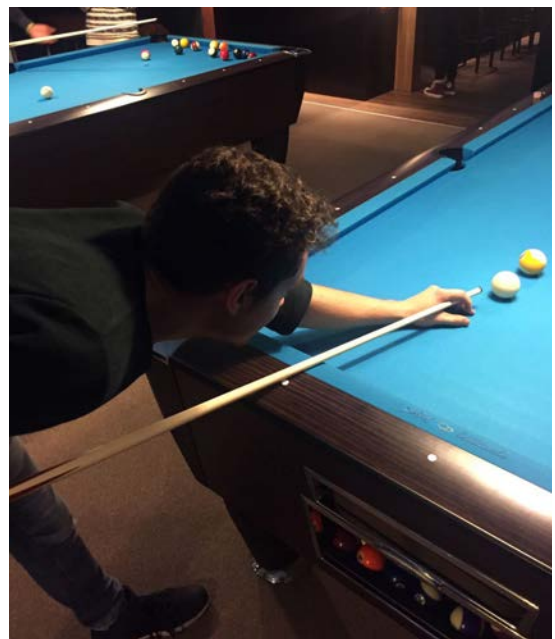


Pool Event

On March 8th, StuCom organised its second fun activity! A big group of CSDB Students came to Pool café Hart van Utrecht to play pool. Before the game started, the locations of this year's CSDB retreat were revealed. By answering the questions during the PubQuiz correctly and thereby collecting letters, you were able to create the words 'Bonn' and 'Cologne'. We were very happy to reveal how we are visiting these two beautiful cities in Germany this year and like to thank you all for your enthusiastic responses!

After the reveal, the competition started. It was nice to see how everybody competed happily with each other and tested their skills at the pool tables. While eating nachos and drinking beers, the atmosphere grew by the minute and we can easily conclude that we all had a very nice evening!

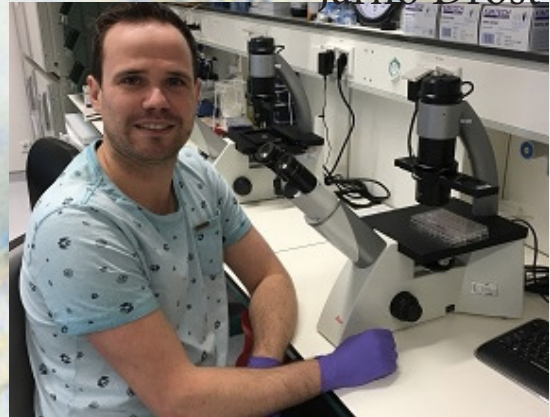
Unfortunately, the pictures that the professional photographer of the Pool Café took have been lost due to an SD-card error. Fortunately, we have taken some ourselves.



Seminar

Jarno Drost

On the 29th of March, the third StuCom seminar was organized. We invited Jarno Drost to talk about organoids in cancer research. Jarno recently started his own lab at the Prinses Máxima Centrum for Pediatric Oncology, where his lab focuses on pediatric kidney cancer. For his research, he makes use of kidney organoids, as organoids turn out to be of great added value to cancer research.



While working in the Clevers Group at the Hubrecht Institute, Jarno Drost was involved in the development of mutated intestinal crypt carcinoma organoids. The intestinal crypt compartments have a high turnover capacity with a lot of crypt stem cells, which makes them suitable for growing organoids. After these first organoid discoveries, it was found that inhibition of Wnt signaling blocks proliferation in crypts. This led to the question whether Wnt is involved in stem cell renewal. It was found that one of the Wnt target genes is *Lgr5*, which is expressed in specific crypt base columnar cells (CBCCs). Using a GFP-Ires- CreERT2 knock-in mouse it was found that CBCCs are located at the bottom of the crypts, intermingled with Paneth cells. The cassette was then converted to one useful for lineage tracing, making use of the visualization of LacZ expression when LGR5 is active. Lineage tracing revealed how LGR5⁺ cells are long-lived and multipotent and how they resemble the stem cells of the small intestine. After culturing LGR5⁺ cells in matrigel with stem cell factors (Wnt, EGF, R-Spondin, Noggin), organoids that mimic the structure of the tissue or tumor they are derived of grew.

Using CRISPR/Cas9, hotspot genes in CRC were mutated. This resulted in triple and quadruple mutants for APC, P53, Smad4, KRas. Quadruple mutant organoids show signs of CIN, which is a hallmark of invasive carcinoma. Injection of the quadruple organoids into immunodeficient mice resulted highly proliferative tumors with carcinogenic features. Another important feature is the capacity of cells to survive in the circulation. In order to study this, the cells were injected in the mesenteric vein of mice, after which the cells should end up in the liver. In triple mutants, no metastasis was observed, whereas with the quadruple mutants, 86% of the injected developed liver metastasis. Thus all 4 mutations are required for sufficient metastatic outgrowth.

The seminar of Jarno really shows how the use of organoids contributes in great extent to different types of (cancer) research and therefore show how useful it could be to exploit organoids for your research.

StuComics

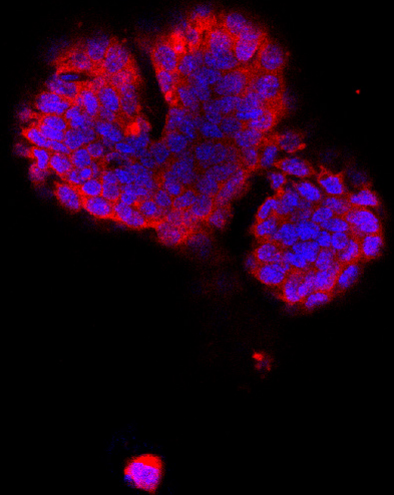


The Smiling Man
Femke Groenveld (1995 -)

Transversal vibratome section of E12.5 mouse, 2016

Also found a piece of art in your
day to day research? Send it in
and you will see it back in the
next newsletter!

stucomcsd@gmail.com



Spread the Love
Margit Bleijs (1993 -)

*Mammary tumor organoid with
estrogen receptor staining, 2017*



Colophon

Editor in Chief

Femke Groenveld

Editors

Rosan Heijboer
Madita Reimer
Elisha Verhaar

Lay-out

Femke Groenveld

Contact

stucomcsd@gmail.com



Hubrecht
Institute

Developmental Biology
and Stem Cell Research



princess
MÁXIMA
center for pediatric oncology



regenerative
medicine
utrecht



UMC Utrecht



Universiteit Utrecht