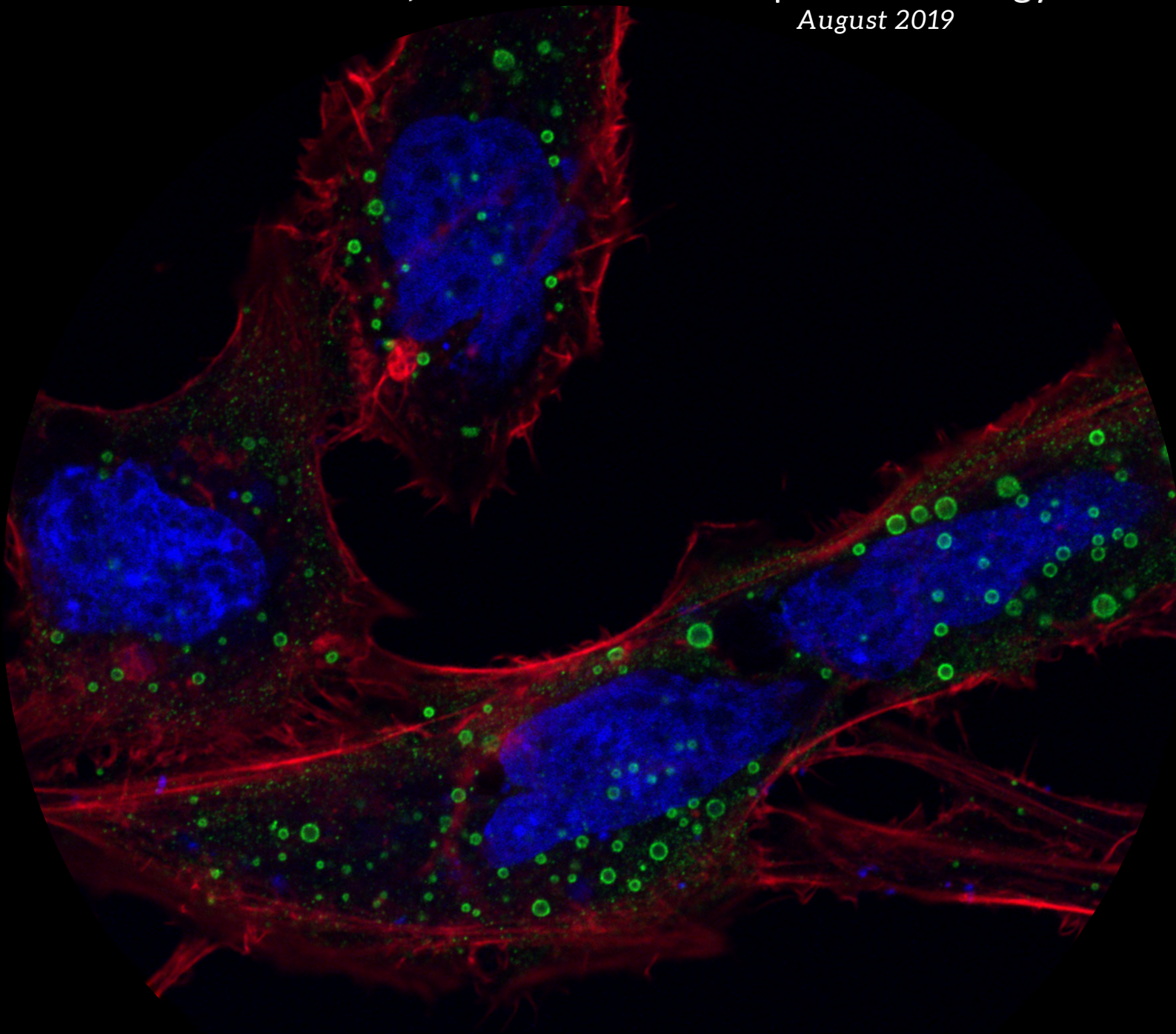
StuCom

Cancer, Stem Cells & Developmental Biology

August 2019



The legendary CSDB Retreat
Heidelberg

An Experience Abroad
Thomas Kluiver in Japan

JULY 2019

SUMMER





Dear CSDB retreat-attendees,

Lucca Derks, widely known to be StuCom 2018-2019's overachieving first lady-of-contact, received a call yesterday from Prof. Dr. Rer. Nat. Habil. Dr. H. C. Bernard Eitel, rector of Heidelberg University. His gravelly voice asked for the overachieving first lady-of-contact who is widely-known to be representative speaker on behalf of the StuCom 2018-2019.

Speaking, she said.

If we could help him out. Lately, such incredible news had reached him concerning this group of remarkable students - not only ravingly positive stories from powerful people of the EMBL; but also from DKFZ came high praise; a company in the city specialized in sleep deprivation had called him with mad enthusiasm; and also from Mannheim, where his aunt had heard from her cleaner who owned a dog which was regular guest in a Karaoke store that dog couldn't stop wagging its tail; he was receiving theatrical Facebook messages from a stupified bus driver from Flevoland. If and when it was possible to bring such another group of excellent, smart, ridiculously beautiful, people to Heidelberg?

Impossible, Lucca said, speaking representatively on behalf of Stucom 2018-2019.

Another such group does not exist.

Thank you all for the wonderful time in Heidelberg/Mannheim!
Love,
StuCom 2018-2019.






AN EXPERIENCE ABROAD

THOMAS KLUIVER PERFORMS HIS MINOR INTERNSHIP AT **RIKEN, KOBE, JAPAN**

The Japanese city of Kobe is probably as unknown to most people in Utrecht as Utrecht is to most people in Kobe (although Nijntje is huge here!). Kobe is most famous for its harbour, its Kobe beef (probably the most expensive in the world) and for housing the developmental biology division of RIKEN, Japan's biggest research institute and my current home.

Before coming here, I worked with Jarno Drost in the Princess Máxima Center where I used foetal and adult stem cell-derived kidney organoids to model paediatric kidney cancer. Before that, I already gained some research experience abroad when I worked in the Nick Barker lab in Singapore on different projects involving LGR5-positive stem cells.

About halfway through my first internship, I started to panic and stress about arranging the inevitable follow-up. I had already set my sights on leaving Europe far behind, and at this point decided that after having worked a lot with adult stem cells, I wanted to try my hand at induced pluripotent ones. Then where better to go than the birthplace of the technique itself? I sent out several mails to Japanese labs working with iPSCs (including Shinya Yamanaka himself), before Minoru Takasato from RIKEN replied to me expressing his mutual interest.

We had a single Skype call and I was in! From there, everything went very smoothly. RIKEN helped me get my visa, flight, residence permit, subway subscription, bank account, a nice room in a share house and even better: reimbursed me for all of that!

The Takasato lab works on the induction of kidney and bladder organoids from iPSCs. These organoids can potentially be used to model diseases, for nephrotoxicity screenings and ultimately as a source of transplantable tissue. In contrast to the adult stem cell-derived kidney organoids from my previous internship, these organoids contain the full range of renal cell types. One of the remaining problems with these organoids, however, is that they still lack a functional duct system that would allow urine to be collected and transported to the bladder. My goal here is to help create such functional organoids from iPSCs by mimicking early kidney development in vitro.

Life in Japan can really be quite crazy. It took me a while after arriving to get used to the specific and unique social etiquette that is expected of anyone. Japan is infamous for its long working hours and cases of karōshi (google that), so I was not too surprised to see my colleagues work long nights and weekends.

My lab is relatively good however, and our sensei, as we call him, is an extremely nice and flexible guy. Nevertheless, every Wednesday at 5.20 pm a voice announces over the speakers that “everyone deserves to go home at this time as Wednesday is not a day for overtime work”. Of course, she gets blatantly ignored by the whole building.

Although the official language of the institute is English, not everyone is as comfortable with that and many meetings are Japanese-only. Luckily, I can fully communicate with most of my colleagues in English. RIKEN also offers free Japanese classes that I attend twice a week. In the past 6 months, my Japanese has improved a lot! Being able to have (basic) conversations and knowing what food I am ordering every night makes being here a lot more fun.

In the evenings and weekends, there is usually still enough free time to explore my city and the rest of the country. I did not expect much of Kobe before I came here but I absolutely love it! The city is shaped like a thin stretch of land squashed between a mountain range (which is home to huge wild boars but still great for hiking) and the ocean. RIKEN is actually located on an artificial island and connected to the mainland by a bridge. Although the downtown area is crazy loud like you might expect from Japan and filled with bars, love hotels and karaoke joints, the rest of the city is surprisingly peaceful. There are some beautiful old shrines and temples, parks, waterfalls, beaches and lots of sake breweries.

BEING ABLE TO HAVE BASIC JAPANESE CONVERSATIONS MAKES THE EXPERIENCE A LOT MORE FUN.

Although the official language of the institute is English, not everyone is as comfortable with that and many meetings are Japanese-only. Luckily, I can fully communicate with most of my colleagues in English. RIKEN also offers free Japanese classes that I attend twice a week. In the past 6 months, my Japanese has improved a lot! I can now express myself and mostly understand anyone I meet around Kobe. Being able to have (basic) conversations and knowing what food I am ordering every night makes being here a lot more fun.

For me, the hardest part of going abroad is having to return home after building a whole new life somewhere. It can also be sad to be without your friends, especially when you pick a place on the other side of the world and they are all broke af. On the other side, being here meant I could meet old friends throughout Asia who were suddenly close enough to visit me! All in all, I feel extremely lucky to have ended up doing the research I love in such a unique place. These kinds of opportunities are so rare! We should take them when we can.

Life in the Lab

CURRENT STUDENTS ON THEIR FIRST INTERNSHIP

It is immensely important and fun to learn from each other about what we are doing in the lab. That's why we want to use this platform to exchange your stories from the lab. As a start, three members of the StuCom who work in different buildings on the Uithof will speak about their internships. But we want to contact other first-year and second-year master's students to tell us about their experiences for the next newsletters. If you are excited about your experiments and want to share them with us, please send an email to **stucomcsd@gmail.com**

Who are you?
I'm Cindy Geerlings. 1st year student.

What is your internship?
II'm doing my major internship in the Galli group in the Hubrecht Institute. In the Galli group we study polyploidy. These are cells that have a replicate of the full chromosome set. There are two non-canonical variations of the cell cycle through which diploid cells can become polyploid. The first is endoreplication, in which S phase and a G phase keep alternating. This results only in mononucleated polyploid cells. The second process is endomitosis, in which cells exit mitosis prematurely before cytokinesis has taken place. This can result in mononucleated polyploid cells or binucleated polyploid cells, depending on the moment of exiting M phase. Previous studies in plants and Drosophila have identified the key drivers of endoreplication (mostly through Cdk1 inhibition), however the molecular factors that control endomitosis are largely unknown. Specifically, it is unclear how endomitotic cycles are initiated and executed, and how cells segregate their chromosomes after multiple rounds of endomitosis. To find drivers of endomitosis I will perform a screen in the K562 lymphoblast cell line, which can be differentiated upon addition of PMA (Phorbol 12-myristate 13-acetate) into megakaryocyte-like cells, which are known to be polyploid. I used this cell line to perform a CRISPRi/a screen to find drivers of endomitosis. In this screen I either activate or inhibit a different gene in each cell and then check by sequencing which genes were important for becoming polyploid.

What are your conclusions?
I just finished sorting the diploid and polyploid cells by FACS. I'll have to wait for the sequencing results of those samples to tell you all about the cool results we (hopefully) got.!

What is the coolest technique you've used?
I think I like the complexity of setting up a complete CRISPR screen the most. But if I have to choose a specific technique it would be FACS. I did a lot of different sorts and I learned a lot about gating and sorting. I think when an experiment is set up in the right way, it is an extremely powerful technique. There is so much information you can get from one Flow Cytometry plot, way more than I knew in the beginning of my project.

What is the most important quality that you learned?
I learned to deal with setbacks.

Would you come back for a PhD?
I really like the topic I've been working on the past months, so for my PhD I would definitely like to stay in the field of cell cycle research.

Who are you? What year are you in?
Robert Becker, first year Master's student

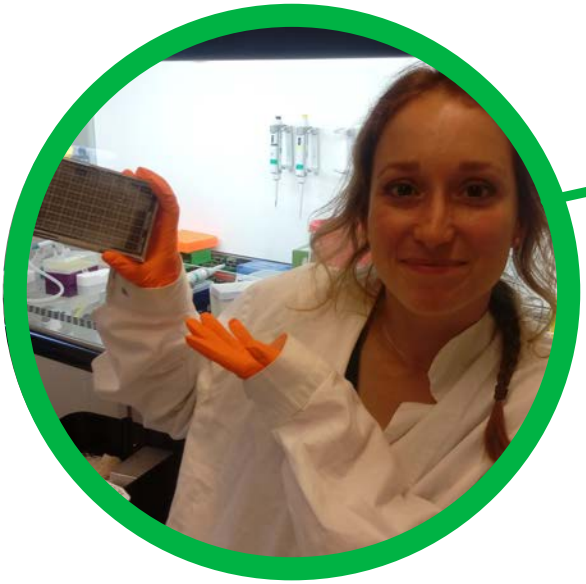
What is your internship?
Kind Group, Hubrecht Institute. We are investigating sequence alterations at repaired DNA double stranded breaks (DSBs) in single cells. If we succeed to show alterations of the DNA sequence at the single cell level, our technique might be used to relate these alterations to the histone context, surrounding DNA, or cell fate. Furthermore, we are using super resolution microscopy to quantify histone dynamics at break sites.

What are your conclusions?
... we submitted for sequencing only last week and are waiting for results. However, the bioanalyzer, which gives us an impression of the distribution of the fragments in our library, looked quite promising. Based on this, we assume our sequencing library will provide us with new insights into alterations or the DNA sequence after DSB repair. Also, I only started this week with analysis of the super resolution images, because processing of the raw images, and merging of the different channels turned out to be very time consuming. Based on my first impression of the data, I am optimistic to find depletion or enrichment of certain histone marks depending on the phase of the DNA repair process.

What is the coolest technique you've used?
The technique we're using to label the DSBs: DamID. DamID was invented to investigate chromatamine interactions. It consists of a methyl transferase fused to a protein; in our case a repair protein. The repair protein targets the methyl transferase to the break site where it deposits methyl groups on adenines in a GATC context. This allows us to identify and sequence these sites specifically.

What is the most important quality that you learned?
Perseverance (!)

Would you come back for a PhD?
Don't ask me that:) I first want to do my second internship in a different environment and on a topic totally different from what I am doing now, before I can take that decision.



Who are you? What year are you in?
Sacha Spelier, 2nd year student

What is your internship?
Minetas, an organ-on-a-chip company. We're trying to set up a triple co-culture model, consisting of endothelial cells; T cells and organoids. Such a platform can be used for studying immunotherapy, and immune checkpoint inhibitors.

What are your conclusions?
So far, we've managed to get a stable co-culture or endothelial cells and tumor cells; and a stable co-culture or endothelial cells and T-cells. Next step is to combine both!

What is the coolest technique you've used?
I think the microfluidic platform or Mimetas is really cool itsself. Establishing co-cultures or multiple cell types is a big challenge (and almost impossible in normal well plates), while such a platform is very valuable for studying mechanisms such as tumor vascularization and T cell migration.

What is the most important quality that you learned?
A company has more rules to obey than a group at university. For example, using cells from a university group could take weeks or paperwork and arrangements. Therefore it's necessary to plan in advance what you want and what you need.

Would you come back for a PhD?
No. Mimetas has quite some PhD students, but I think doing a PhD in a company is quite different from doing in the academic world. It's more goal-centered, and less centered around, really finding out how something works.

StuCom Seminars Recap

April Seminar: Scientists in Academia & Industry

On April 23rd, StuCom welcomed 2 scientists on the merging lines between academia and the industry: **Lieke van Zogchel** who works on a collaborative project between PMC and Sanquin and **Raimond Heukers**, a postdoctoral fellow in Molecular Pharmacology group at the VU University in Amsterdam and a scientist at QVQ Holding BV, Quality in Antibodies.

Lieke's talk, apart from her current project on developing diagnostic "toolbox" (for either early detection or relapse of neuroblastoma) based on circulating cell-free DNA, also touches upon the unique working environment at Sanquin.
Many research groups at Sanquin focus on both fundamental blood research and developing toolboxes/ clinical products based on plasma, or in short, try and make something useful out of the blood bank available The income from these products and grants will go back to the lab for more developments and fundamental research. Because of the varieties of kits available at Sanquin, there are many collaborative projects where academic groups, for example, PhDs at PMC use the kits developed by her/groups at Sanquin.

Raimond did his PhD at the Paul van Bergen en Henegouwen Group, Faculty of Science on using nanobody (VHH) to study how modulating receptor internalization can be used as a (cancer) therapeutic. VHH/single domain antibody/nanobody can be very useful due to its small size, simple production and high affinity. At QVQ, with a small team of 10 people, they work in collaboration with research groups in universities, and make VHH/ VHH-based products for bigger pharma companies, etc. with a focus on using VHH for imaging.
From his experience, he shared with us that working in the industry will be different from in a lab in some aspects such as more restricted working hours, less student supervision, and more choices of projects (unlike a research line in a lab)..

July Seminar: On Scientific Writing

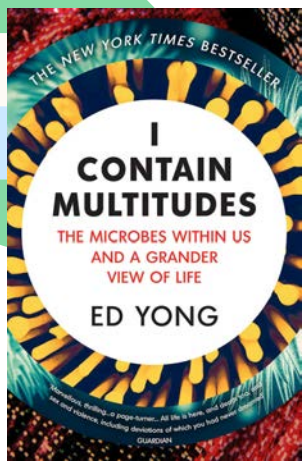
For July's seminar, StuCom invited **Dr. Ellen Wehrens**, a scientific writer in the Rios group at Princess Máxima Center. How do you find yourself in such a position, quite rare in the Dutch scientific world? After bringing her scientific career to a successful start, Ellen explained, she realized that her potential and passion lay more with writing and persuasion than with more lab work. The Rios group took the chance, thinking: if Ellen brings in two grants, that's enough compensation for her own work and more.

Hereafter, she summarized some tips to tackle scientific writing, quite convenient for our upcoming internship reports: think before you write, start with a plan, don't write and rewrite at the same time.
P/s. check out scientificwritingtips.com

YOUR FAVORITE SCIENCE STUFF

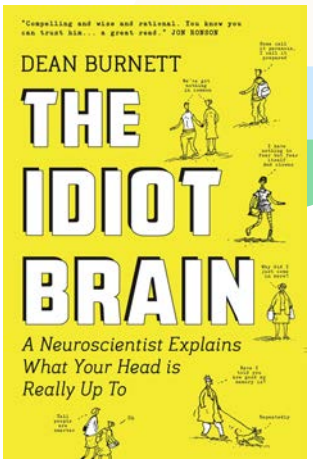
ON THIS PAGE WE SHARE SOME OF OUR FAVORITE SCIENCE CONTENT ON THE WEB OR ELSEWHERE. BUT WE WANT TO KNOW WHAT YOU LIKE! SO PLEASE SHARE WITH US YOUR FAVORITE STUFF AND GET IT ONTO THIS PAGE IN THE NEXT NEWSLETTER!

MAIL TO **STUCOMCSD@GMAIL.COM**



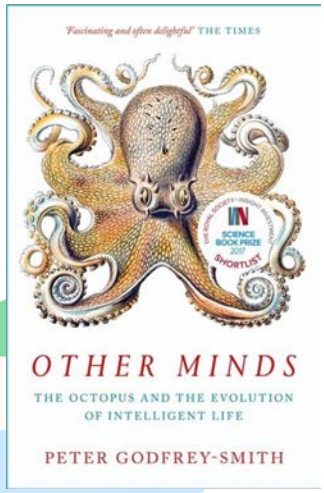
I Contain Multitudes: The Microbes Within Us and a Grander View of Life - Ed Yong

In I Contain Multitudes, Ed Yong opens our eyes and invites us to marvel at ourselves and other animals in a new light, less as individuals and more as thriving ecosystems.



The Idiot Brain
A Neuroscientist Explains What Your Head Is Really Up To
- Dean Burnett

Expertly researched and entertainingly written, this book is for anyone who has wondered why their brain seems to be sabotaging their life, and what on earth it is really up to.



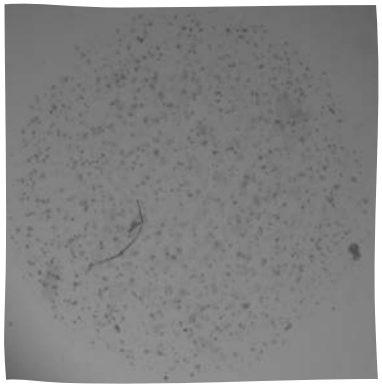
Other Minds
The Octopus and the Evolution of Intelligent Life
- Peter Godfrey-Smith

The octopus is the closest we will come to an intelligent alien meeting. What can we learn from the encounter? In Other Minds, Peter Godfrey-Smith, a distinguished philosopher or science and a skilled scuba diver, tells a bold new story of how nature became aware of itself - a story that occurs largely in the ocean, where animals first appeared.

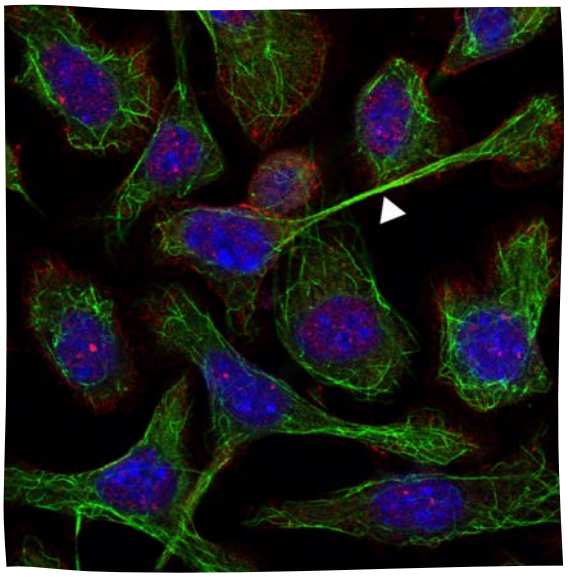
WALL OF FAME N SHAME

Nothing in science is more important than sharing your knowledge. Here at StuCom we take that very seriously. On here, for every newsletter, we are going to showcase some of the best and some of the worst that we, CSDB students, have produced during our internships. Together on one page, so that you can determine for yourself what is successful and what is.... less so.

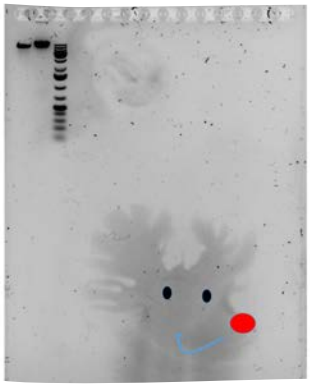
The best picture we get will be featured on the front page. Share your own achievements with **stucomcsd@gmail.com**



When your organoids don't grow but you hair does.
- by Dimitris Laskaris



Kep1-11 cells negative for E-cadherin cannot form adheren junctions, hence, afadin (red) localizes to the nucleus (blue). Microtubules are stained in green.
- by Kirsten Veltman



Peek-a-boo! from Rudolph, the reindeer.

- by Madalena Tropa Martins

```
if [[ $SV_CALLER == *"nanosv"* ]] || [[ $SV_CALLER == *"NanoSV"* ]]; then
  MAPPING_ARGS="-t $LAST_MAPPING_THREADS -r $REFGENOME -rd $REFDICT -l $LAST_DIR -ls '$LAST_MAPPING_SETTINGS' -s $SAMTOOLS"
  for FA in $CANDIDATE_DIR/*.fa; do
    echo $FA;
  done | \
  xargs -I{} --max-procs $THREADS bash -c "bash $PIPELINE_DIR/last_mapping.sh -f {} $MAPPING_ARGS; exit 1;"

elif [[ $SV_CALLER == *"sniffles"* ]] || [[ $SV_CALLER == *"Sniffles"* ]]; then
  MAPPING_ARGS="-mm2 $MINIMAP2 -oc -mm2s '$MINIMAP2_SETTINGS' -r $REFFASTA -t $LAST_MAPPING_THREADS -s $SAMTOOLS"
  for FA in $CANDIDATE_DIR/*.fa; do
    echo ${FA/.fa/};
  done | \
  xargs -I{} --max-procs $THREADS bash -c "bash $PIPELINE_DIR/minimap2_mapping.sh -f {}.fa -o {}.sorted.bam $MAPPING_ARGS; exit 1;"
fi
```

This code in Bash checks if I want to run either SV caller "NanoSV" or "Sniffles" and then specifically calls a corresponding mapping algorithm to map all the reads you got with Nanopore sequencing in parallel
-by Sam de Blank

COLOPHON

STUCOM E-MAIL
stucomcsd@gmail.com

STUCOM FACEBOOK
Stucom CSND

CSDB INSTAGRAM
CS&D Master Students & Alumni

CSDB LINKEDIN
CS&D Master Students & Alumni

FRONTPAGE PHOTO
The front page shows Axin puncta by Enya Vermeulen

This StuCom newsletter was written and designed by Tran Ngoc Minh Thi and Niels Tjoonk unless otherwise specified. Thanks to Dimitrios, Cindy and Joost for the retreat pictures.