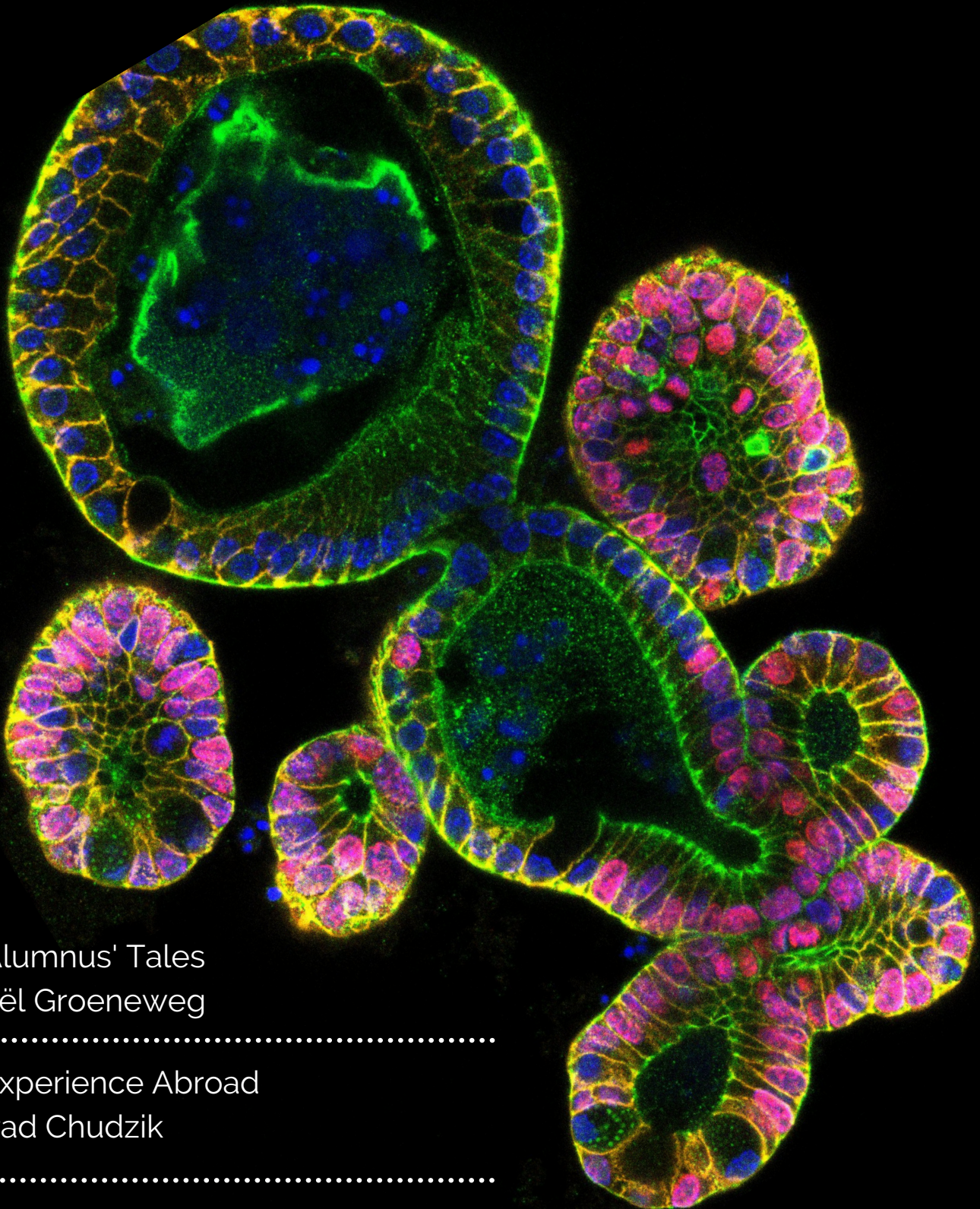


StuCom

Cancer, Stem Cells & Developmental Biology

February 2019



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StuCom seminar

To study the origins of cancer, Ruben van Boxtel explores the mutational landscape of cancer cells for clues. This and more he explained to CSnD students in this year's first StuCom Seminar.



What causes cancer? We know the extrinsic and intrinsic risk factors that correlate with cancer: lifestyle, toxic carcinogens, inherited genetic factors. But these do not explain fully why people get cancer. Is the rest bad luck?

Ask Christian Tomasetti and Bert Vogelstein and they will tell you yes. Because, as they argue in a 2015 Science paper, the incidence of cancer types correlates with stem cell division rates of the organ it occurs in. If this is true, Ruben van Boxtel states, then organ-specific mutation accumulation may reflect cancer incidence as well. If so, which processes are involved in creating these mutations? Whichever they are, these are the processes we must focus on to cure.

By smartly using organoids to grow out single stem cells, you can generate enough DNA for accurate sequencing. Due to the clonal nature of the organoid, the sequencing results show the genetic makeup of the single original stem cell. This method supplied the team of Ruben with unprecedented information about mutation accumulation in healthy stem cells of the liver, the small and the large intestine. What was discovered was that mutational accumulation in all three organs was the same and does not reflect the variation in cancer incidence in these organs. Importantly, however, the type of mutations found in each organ was specifically different, and this pattern works as a footprint reflecting the type of the mutagenic processes involved in each organ.

So, as Ruben tells us, it is organ-specific mutagenic processes that create variation in cancer incidence between organs. And you can analyze the mutation patterns in the DNA like footprints, to identify their nature. Revolving around this premise, the group of Ruben will track the 'mutational footprints' to study the origin of cancer.



On November 27th a group of over 40 current and alumni CSnD students gathered for a lecture by Ruben van Boxtel, group leader at the Princess Maxima Center for Paediatric Oncology, Utrecht. Afterwards, with pizza and drinks at hand, the students and the speaker mingled with some interesting conversations as the result.

Susanna van den Brink, a final year PhD candidate in the Van Oudenaard group, will present for the next StuCom seminar

The next StuCom Seminar will be given on Monday February 11th at 18:00 in Stratenum 2.106/2.112

December Activity: SinterChristmas Pubquiz



On December 11, 2018, CSDB second and first-year students joined forces to conquer the challenge of StuCom pub-quiz while enjoying a handful of beers at Utrecht's good old Irish pub, Mick O'Connells. All 5 teams did an amazing job at quizzes about Utrecht, music from various eras, distinguishing elbows & asses, and recognizing Stucom members from their baby pictures! The best part of the night is everyone won and got their well-deserved Christmas presents!



Excited about the next StuCom Activity? Mark your calendar on March 18th





AN ALUMNUS' TALES

DANIËL GROENEWEG WORKS AT **ABBVIE** AS
AS AN ASSISTANT CLINICAL RESEARCH
ASSOCIATE

Hi everyone,

As alumni of the CSnD master program I've been asked to write a little piece about my professional career after my graduation. As a student I've always been interested in career. During my study time I've helped organizing the Mebiose career day event as president in 2014 and I joined on study trips to e.g. Basel and Heidelberg. I did not know what path I would choose, before I started my master program, but below is my story.

I've started my master in biomedical sciences, because I really like the bachelor Biomedical Sciences and was keen on getting to know what the practical side of research actually is. I joined Prof. Sluijters lab in the UMC Utrecht for my major research project, researching the role of transcription factors during cardiac development and disease. My minor internship was focused on the maturation process of embryonic stem cells towards cardiomyocytes at Harvard Medical School associated with the Massachusetts General Hospital.

and my thesis was performed in the Bakkers lab (Hubrecht) at cardiac regeneration in zebrafish.

At the end of my master program, I decided that after two years of internship I had seen enough of research. The question was: 'to PhD or not to PhD?'. I always had in mind to do a PhD, but since I was still doubting research so much at the end of my master and seeing some people struggle with their Ph.D., I've decided not to Ph.D. So having answered this question, another question arose: 'What else?'. I had a little bit of knowledge of what was outside academia; because of the career day I've organized in combination with visiting several companies during study trips. However, a lot remained unknown about the medical/pharmaceutical world outside academia.

Browsing on LinkedIn one day, I saw an advertisement of an old lab colleague from the UMC Utrecht who was then working as a recruiter within life sciences. She was going on pregnancy leave and they were looking for her replacement. The ad said they were looking for an enthusiastic, social and scientific person who wanted to help other people get a job. I texted her that I was interested and wanted some more information. We had

coffee in a bar in Utrecht and I got really excited about this opportunity. At one hand, there was a chance to get an actual paid job. On the other hand, this was a great opportunity for me as well to orient myself in the pharmaceutical world. As a recruiter I could see different jobs, different companies, meet a lot of new people and learn about their career choices. I got a contract for a year, but after six months I already had the feeling this job wasn't fulfilling my ambition. So I decided that I would look for a different job, more related to my educational background than this job actually was.

I've contacted many people via LinkedIn or via my old Mebiose network to drink coffee and listen to their stories. I was getting really interested in Medical Affairs and Clinical research. Therefore I decided to apply for Medical science liaison and clinical research associate functions. I liked the idea of working on an intellectual item again and contributing to improving the human body. All medicines in the market have gone through a lot of clinical studies in order to be accepted by medical ethical committees (FDA/EMA). I've contacted many agencies (such as The Clinical Companies where I'm working for now) and had a lot of interviews, but often I got rejected due to my lack of experience. Luckily AbbVie gave me the chance to start as assistant CRA seconded via The Clinical Company.

As a clinical research associate, you are responsible for clinical trials in different hospitals. AbbVie is mainly working on neurology, virology, immunology, and oncology. We have several new medicines in development, for which we need a lot of clinical data before they can be accepted by the medical ethical committee and the governmental institutes. I'm responsible for submitting and getting approval for clinical trials, for selecting sites that will be enrolled in our studies, for sites being compliant to our study protocol and to make sure clean data is obtained from the sites. We obtain a study protocol from our headquarters and they ask us to start recruiting hospitals (also called sites). We try to include doctors who are experts in their field. Therefore we are mostly working with academic and/or top clinical hospitals. Once a site is selected, all contracts have to be made in order and site staff has to be trained on the protocol provided by

us. Then the sites will start screening patients and if patients are eligible to be included in a study (based on in-/exclusion criteria) a patient can be enrolled in the study. Until the end of a study, which can be 2 years later, I'll be responsible for the site to be compliant to our protocol and that the patients' safety will not be in danger.

In this job I really like the idea of contributing to science on a different level. Our medicinal products are biologicals that interfere on several receptors and/or pathways, which we learned about during biomedical sciences. The fact that you can really see that a product is working or not in a human body is the most direct answer that can be provided on a question regarding development of a new medicine (but it takes years...). Currently, I'm working on immunology studies, since they are simpler than oncology studies and I've just started my career as a CRA. In the coming years, I would love to run oncology studies and become an experienced CRA. I hope that I will get a better view on the pharmaceutical world of medicine development and see what next career opportunities will be.

Best of luck with your career choices and I hope my story shows you some different aspects of a career outside the academic world. I would suggest to always be networking and always be polite and respectful to other people. I believe that that will improve your chances of getting unique opportunities the most.

Feel free to contact me!



Daniël Groeneweg
Assistant CRA AbbVie
<https://www.linkedin.com/in/dsgroeneweg>

Get to know StuCom '18 - '19



Big Boss #1: Madalena Tropa Martins

Filled with humor & wit,
Madelena gives out the positive
energy that keeps all StuCom
meetings & deadlines in order
& in the funniest way possible!

@ Kuiper Group, PMC



Big Boss #2: Ramon Barrull Mascaró

Beside his love for Muse, Ramon
also loves fighting for the
cheapest deals for StuCom
Retreat, running the meetings &
organizing seminars.

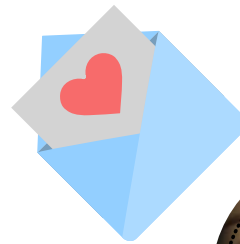
@ Maurice Group, UMC



Missy Treasurer: Anna Pagliaro

Our very lovely Anna. Don't be
mistaken by her friendliness &
charisma; if you try to steal
some money from Stucum,
she'll make sure you're well
"taken care of."

@ Coffer Group,
UMC/Hubrecht



Wanna reach us? Ask Lucca Derks

Since StuCom is very busy (?), you
have to go through Lucca first.

She's got a talent for cooking,
giving out catchy emails & working
at 200% efficiency when hungover.

@ Gloerich Group, UMC



Pretty Little Noties: Mara Bouwman

With an aesthetic soul, Mara not only makes StuCom minutes pretty but social activities super duper fun too! Her typing speed can catch up with Eminem & her cooking skill is over the top!

@ Bakkers Group, Hubrecht



The Clown on the Cloud: Niels Tjoonk

If you want a joke (good & bad) or a guide to the off-the-beaten-path side of Utrecht, find Niels. This funny fella goes out of his way to make sure StuCom is represented in the best way possible (logo, posters, newsletter ...)

@ van Boxtel Group, PMC



Master Multitasker: Marc Trani

Born on Christmas' Eve, God-like Marc can accomplish all tasks of organizing retreat, seminar & social activities in a heartbeat. An avid dancer & passionate lover of music too!

@ Clevers Group, Hubrecht



StuCom's Greek God: Dimitrios Laskaris

Involved in running StuCom's everything, seminars, social activities & retreat, Dimitrios usually unwinds with his piano. You might see him on stage @ open nights somewhere!

@ Snippert Group, UMC



Crazy Poor Asian: Tran Ngoc Minh Thi

Sometimes she designs; sometimes she organizes seminars; most of the time, Thi gives out the greatest of hugs :)

@ Maurice Group, UMC



AN EXPERIENCE ABROAD

KONRAD CHUDZIK FOLLOWS AN INTERNSHIP IN THE MAX PLANCK INSTITUTE FOR MOLECULAR GENETICS IN BERLIN

My name is Konrad - I come from Gdansk in Poland. I joined the CSnD master program in February 2017. I

did my major research project at the lab of Jacco van Rheenen at the Hubrecht Institute and partly in Hugo Snippert's group at the UMC. I worked with small intestinal organoids to explore questions about the impact of APC mutation on stem cell competition inside the stem cell niche and on the subject of crypt fission and fusion. This was a great experience and I enjoyed my time at Hubrecht Institute very much, but for my minor research project I was very interested

in (epi)genetics and I wanted to go to Germany, so I browsed the internet for groups that matched my criteria and I decided to apply to a group of Stefan Mudlos at Max Planck Institute for Molecular Genetics in Berlin. His group looks at the impact of structural variants on gene expression using limb development. I sent an e-mail to Prof. Mudlos and fortunately, I was contacted by a post-doc from his lab who was looking for a master student. We did a Skype interview, then he sent me some papers and related documents, so I could get a better idea of

what I would be working on, and after a month we did another Skype call after which we both agreed to work together.

I started planning my internship very early as I wanted to start in June of 2018 and I already sent my application at the beginning of August 2017. Still, my internship only got approved around November. This gave me more than enough time to arrange all the necessary things regarding the internship, as traveling within EU doesn't require a lot of effort, but it was nice having a bit of extra time. This allowed me to properly explore financing options - in the end, I only went for the standard Erasmus grant - and to look for accommodation. Getting a place to live in Berlin is difficult - harder than in Utrecht in my opinion - and Germans are very strict about their paperwork, so it was good that I had plenty of time to take care of that. In general, it would certainly be possible to plan the internship in a much shorter time, but I also see no downside to doing it early.

AS TO BERLIN: THE JOKE GOES THAT BERLIN IS NOT GERMAN.

Right now, I am working on doing multiple knock-ins at a locus that has an interesting configuration of TADs and LADs. We are hoping that tinkering with this locus might help us address questions regarding the role and function of TADs and LADs and elucidate important information about the folding of the genome. We use a CRISVar protocol developed in Mundlos lab to relatively quickly generate transgenic mice in which we look at limb development, which in turn is a readout of gene expression. I enjoy working on this topic and I have a great supervisor. I have been offered to stay in the lab for a Ph.D. and I accepted. Hence after I finish the minor research project and graduate, I will stay in the Mundlos group and continue working on this topic.

As to Berlin: the joke goes that Berlin is not German. It is extremely diverse, very lively, with massive amounts of events, places to go etc., but on the downside it is quite dirty, unorganized and unkept with plenty of small inconveniences. Additionally, as I mentioned above, the housing situation is not good and it is getting worse every year with no solution in sight.

If I were to give one tip to students who want to go abroad: talk to people, friends, other students, alumni, professors or whomever, who has been in that country, particular city, institute etc. Even if they cannot tell you anything relevant for you, there is a high chance that they can refer you to someone who will.

Editor's note: Professor Dr. Stefan Mundlos is the head of the Development and Disease Group of the Max Planck Institute for Molecular Genetics in Berlin. From the webiste:

About the Mundlos group

"We analyse human genomes from individuals with malformations by Illumina and other technologies to identify disease causing variants. A range of bioinformatic tools are applied for genome analysis, 4C, HiC and other applications.

Our questions, our goals

How are genes regulated and how is this related to 3D folding of chromatin? How do enhancers work and how is their activity influenced by epigenetic modifications?

And, finally, how are these processes related to disease? Ultimately, we want to understand the cause and pathology of human abnormal development (malformations) in order to develop better diagnostic tests and/or for treatment. The effect of variants in the non-coding genome is currently difficult to predict. We want to understand mechanisms of gene regulation during development to better understand how abnormal gene regulation can result in disease."

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



out that we shared the same opinions on the goals of the internship. My daily supervisor in particular is a lot like me, and we really clicked while discussing her research, which is why I chose for this lab!

Who are you?

My name is Lucca Derks, I come from Nijmegen and have spent the last four years in Utrecht. I spent my last year partly in South America and I have slowly gotten used to the full-time schedule again. I will probably apply for a PhD position after this master's programme, but before that happens I hope to spend some months on the other side of the world again.

What is your internship?

My internship is in the group of Martijn Gloerich, part of the Center for Molecular Medicine in the UMC Utrecht. I am working on a familial type of gastric cancer, where inactivating mutations in E-cadherin are the initiating event. We mimic the mutation in organoids of gastric epithelium, and hope to elucidate why these patients develop gastric cancer due to a mutation in a very general component of the adherens junction.

How come you're doing your internship here?

I applied for different labs, based on what techniques they were using and what their subjects were. After interviewing with the PI and my potential supervisor, I found

What is the coolest experimental technique that you're going to do?

The last couple of months I have tried to learn how to keep my gastric organoids alive and well (a struggle for both me and my supervisor haha), besides knocking some genes in/out in cell lines (which I hope to do in my organoids as well in the future). I am mostly working with a confocal microscope for immunofluorescence assays, but will also use qPCR and Western Blotting to investigate the activity of signaling pathways in the future.

Tell me two things that you love about your lab group.

My fellow CSDB students in the lab of course (we like to think that our supervisors are co-parenting all of us)! Besides that, everyone is available for help or advice, as we are working with quite different techniques, so you can really learn a lot!

Which three adjectives pop up immediately when you think about your lab?

Good atmosphere, young, creative (you should see the stretch devices that are made to study mechanotransduction in epithelial cells!)

How is the community spirit at your institute?

We have a weekly borrel and monthly theme borrel, so even though our department is spread over two different floors, we do see each other frequently. Also, we have two weekly meetings, where current research is presented. Therefore, most of the staff is pretty up-to-date with the research throughout the department!



Who are you?

Ha peeps! My name is Niels Tjoonk and I was born amongst cows in Vorden, which is a little town in the eastern wastelands of the Achterhoek ('Behindcorner'). I've felt at home in Utrecht for a while now.

What is your internship?

I started my first internship this September at the Princess Máxima Center for Pediatric Oncology, in the lab of Ruben van Boxtel. The project I'm doing is on pediatric acute myeloid leukemia (AML), and more specifically on a subtype which is characterized by a fusion protein called RUNX1-ETO. The group has found evidence for oxidative stress in the genomes of these cancers, and I'm going to see whether I can reproduce these findings in an experimental setting. Gene editing and next generation sequencing will be my main tools of choice.

How come you're doing your internship there?

I chose this lab group because I knew Ruben from my BSc thesis and in my gut it felt right. But a different reason is that I expected the environment to be exciting and open. The Princess Máxima Center is a new institution in a new building, and Ruben is a young PI with a group of young people who are taking on new jobs or projects as well. That sounded to me like fertile ground to get into contact with a lot of people easily, and learn volumes.

What is the coolest experimental technique that you're going to do?

I still think everything is cool <3. Wetlab-wise I'm a real newbie. But I look forward most to using Cas9 base editing and mutational signature analysis of whole genome sequencing data.

How is the community spirit at your institute?

Because more than half of the building is a hospital for fatally ill children, you really need to not get tangled up in despair. The Princess Máxima Center reacts to the somber reality of the children's illness by focusing instead on the better times when the children are giddy and playful. They designed the building and the policy vision with that in mind. You can kind of feel that when you walk in. Also in the research department. Adjacent to the entrance is a playdoh-textured statue of a young child riding a crab, which sums it up pretty nicely. So part of that aim is to realize a friendly, social atmosphere that stimulates teamwork and a community spirit. And as far as I can see, that works.



Who are you?

Hello hello. My name is Mara. I'm from Voorschoten, a small town close to Leiden. After CSND, I'm not entirely sure what I want to do, but I'm considering a PhD.

What is your internship?

I started my first internship in the group of Jeroen Bakkers at the Hubrecht Institute.

How come you're doing your internship there?

During my Biology Bachelor's here in Utrecht, I already got a glimpse of the work they do with zebrafish during a tour of the aquarium, and I believe it even was my current supervisor who led that tour back then. I learned that zebrafish are able to regenerate their hearts after injury, and that studying the underlying processes might bring us closer to treatment of human heart diseases. I was so amazed by this research, that after being admitted to the Master's programme it was the first application email I sent. Luckily, Jeroen offered me an internship position on this exact topic!

Currently I'm working with various mutant zebrafish lines to study the roles of specific genes in heart regeneration. So far, I'm really enjoying the lab work as well as working with zebrafish as a model organism in general. I feel like I'm learning more than my whole bachelor's put together!

What is the coolest experimental technique that you're going to do?

I get to do some cool things like heart extractions, cryo-sectioning and working with different microscopes.

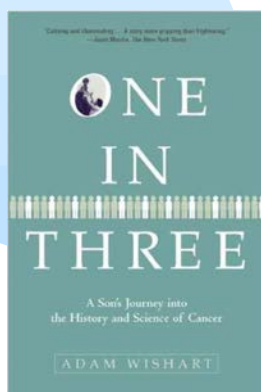
How is the community spirit at your institute?

I think the Hubrecht Institute is a great place to do an internship, since there are a lot of possibilities for master's students to be involved in interesting, relevant research. I also really like the environment in the lab, and I feel really included in the group. I even got to be part of the 15 years Bakkers lab reunion, and we went to a Christmas market this December. All together I'm having a great start at my first internship!

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**



One in Three: A son's journey into the history and science of cancer.

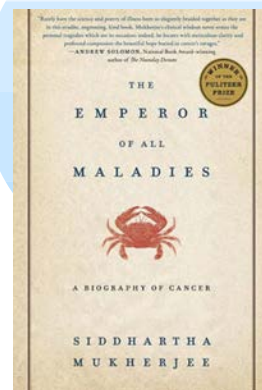
Adam Wishart

The cancer diagnosis of his father drove Adam Wishart to understand what was going to happen, why and how. He and also his father needed to know, in order to deal with the disease and maintain sanity. He could not find the book, however, that could explain his basic questions: what is cancer? why do we get it? why is it so difficult to cure? So he dove into the science, and wrote it himself.

Cancer: the emperor of all maladies

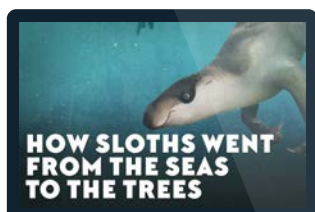
Siddhartha Mukherjee

Highly enjoyable because it interweaves biological breakthroughs in cancer research with public opinion, laws and regulations, religion, funding and personal stories of an oncologist. Not only a book, but also a great documentary mini-series by the master filmmaker Ken Burns



Eons

PBS studios, YouTube

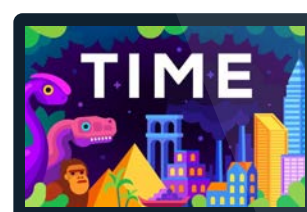


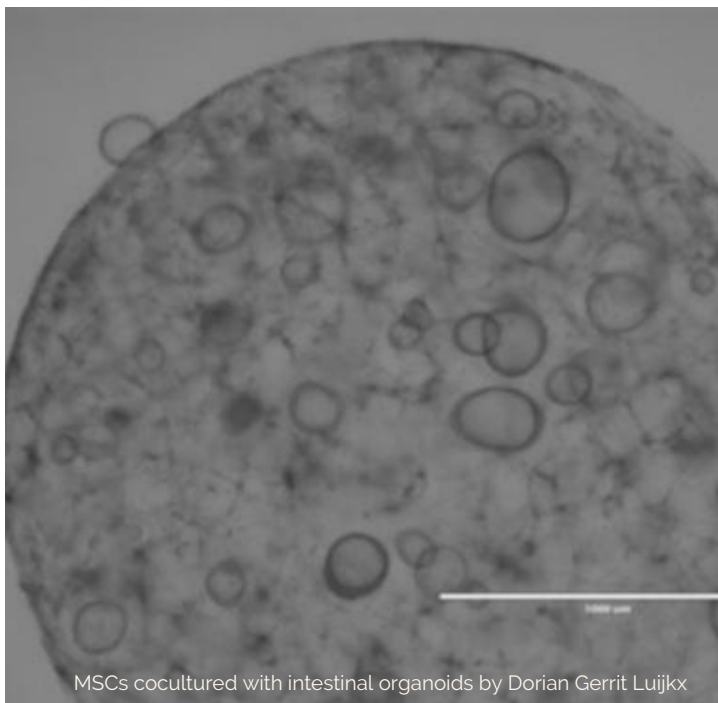
Four billion years of life on this earth must have created some amazing stories. Sea-dwelling sloths. How blood evolved. When the earth was purple. Dinosaurs. These and myriad other stories are told weekly in bite-size videos with beautiful artwork.

Kurzgesagt – In a nutshell

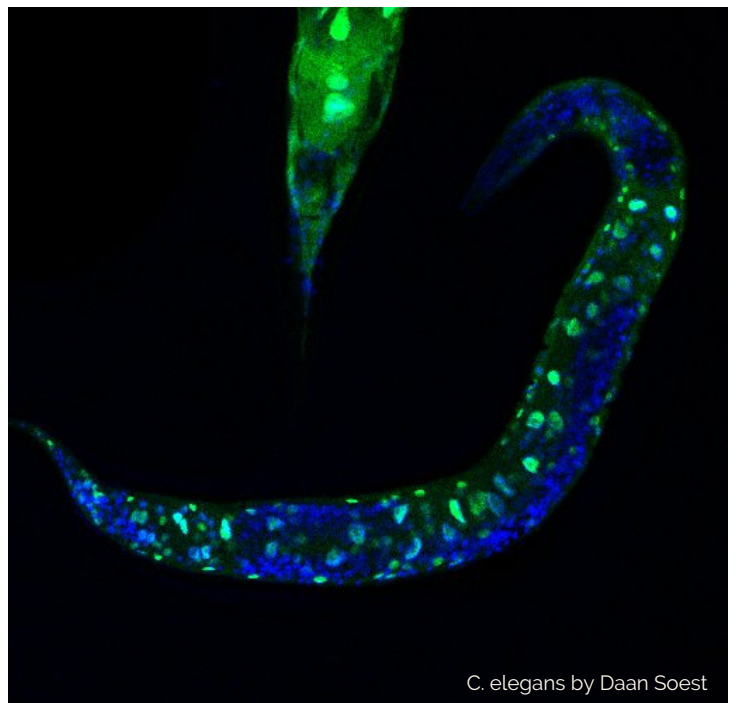
YouTube

This channel tackles mind-boggling scientific concepts with impressive clarity and some of the best (and cutest) animation on the internet. If you want to learn about space elevators and Dyson spheres, or wander about what the end of the universe looks like, or see bacteriophages in another light: do you have 10 minutes?





MSCs cocultured with intestinal organoids by Dorian Gerrit Luijkx

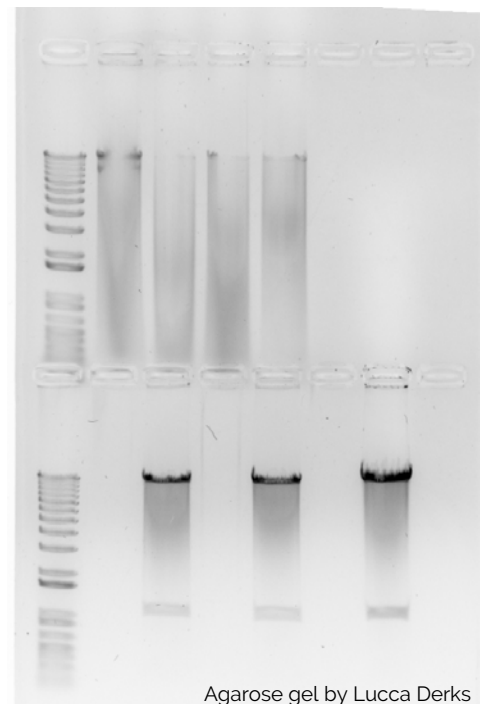


C. elegans by Daan Soest



Zebrafish by Mara Bouwman

WALL OF FAME N SHAME



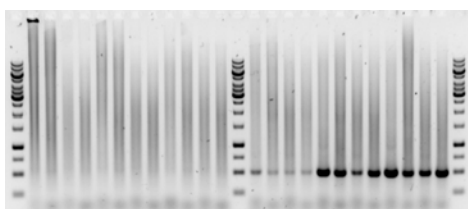
Agarose gel by Lucca Derks

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.

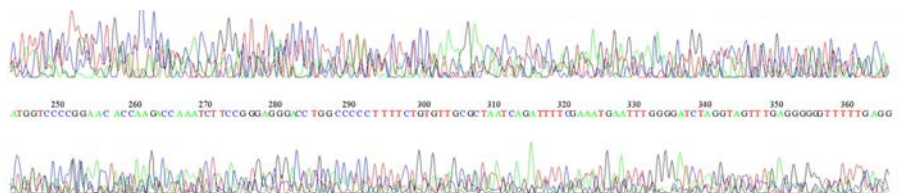
The best picture we get will be featured on the front page. Share your own achievements with **stucomcsd@gmail.com**



Heart-broken by Thi Tran



Aga-gross gel by Niels Tjoonk



Sequence in horror by Thi Tran

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CS&D Master Students & Alumni

FRONTPAGE PHOTO

The front page shows the winner of the picture challenge, "Organoid-man" by **Judith Veldhuizen**.

This StuCom newsletter was written and designed by Tran Ngoc Minh Thi and Niels Tjoonk unless otherwise specified.

FINAL THOUGHT

Sonnet-To Science by Edgar Allan Poe
(1829)

*Science! true daughter of Old Time thou art!
Who alterest all things with thy peering eyes.
Why preyest thou thus upon the poet's heart,
Vulture, whose wings are dull realities?
How should he love thee? or how deem thee wise,
Who wouldst not leave him in his wandering
To seek for treasure in the jewelled skies,
Albeit he soared with an undaunted wing?
Hast thou not dragged Diana from her car,
And driven the Hamadryad from the wood
To seek a shelter in some happier star?
Hast thou not torn the Naiad from her flood,
The Elfin from the green grass, and from me
The summer dream beneath the tamarind tree?*

