RESCUE

Regenerative Medicine
Training Network

UMC Utrecht

Utrecht University

Hubrecht Institute

RESCUE: advancing regenerative

In 2019, a group of 31 young, international researchers from 17 countries started their PhD projects at Utrecht University. The REgenerative medicine and Stem Cell technology in UtrEcht (RESCUE) training program was funded by a Horizon 2020 Marie S. Curie COFUND grant. This European Union project aims to stimulate researchers' international mobility. Now, in 2023, the students are finalizing their PhDs. In this booklet, we celebrate their achievements as they reflect on these past years.

With an aging population, a growing burden of chronic conditions, and rising healthcare costs in Europe, the need for organs, tissues, and personalized strategies for decision-making in therapeutic choices has never been greater. Developments in areas such as 3D-bioprinting, induced pluripotent stem cells (iPSC), complex organoid cultures, and gene editing, herald the promise of regenerative medicine technologies. These advancements offer prospects for applications such as clinical transplantation or personalized assessment of treatment efficacy.

These new model systems and methods have also opened paths toward deeper knowledge of the body's own regenerative healing processes, and the means to direct them. However, for regenerative medicine to fully capture its potential, a synergistic and multidisciplinary effort remains necessary to achieve essential scientific breakthroughs.

"The need for organs, tissues, and personalized strategies for decision-making in therapeutic choices has never been greater"

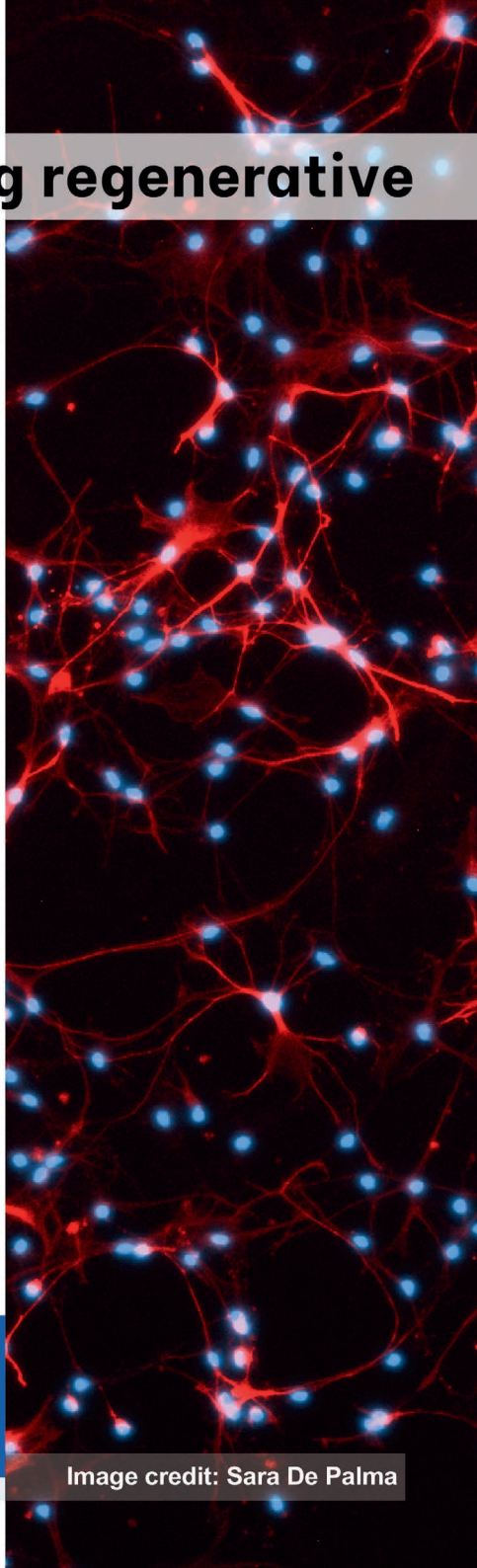
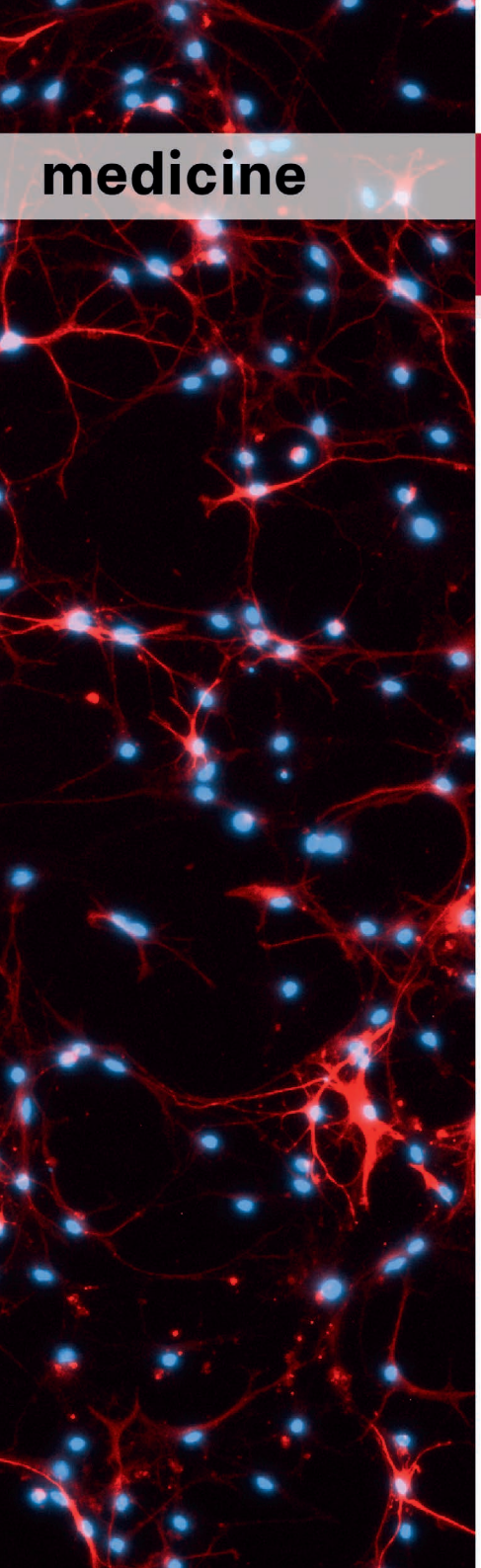


Image credit: Sara De Palma



medicine

"The RESCUE PhD students were a diverse community whose presence has bolstered the Regenerative Medicine Program in Utrecht"

Through the years, the RESCUE students helped build a connection with the future generation of regenerative medicine researchers worldwide. They joined 18 departments at Utrecht University, the UMC Utrecht, and the Hubrecht Institute, but came together working at the recently opened Regenerative Medicine Center Utrecht. Alongside their research, the PhD candidates took part in a broad educational program that covered topics from microscopy and stem cell function to ethics.

The long-term objectives of this initiative were to empower the unique research environment in Utrecht, and also strengthen the international regenerative medicine network in a continuous and lasting manner. The RESCUE students were a new, diverse community whose presence has bolstered the growing Regenerative Medicine Program in Utrecht and helped to put it on the map.

This booklet provides an insight into the variety of innovative research projects in the field of regenerative medicine. From organ-on-a-chip kidney models to surgical implant technology that prevents infection and vascularized tissue grafts. Also, you will read about the students' personal journeys and future aspirations. In closing, we extend our congratulations and gratitude to these young scientists who have enriched our community.

Prof. Paul Coffer
Chair, Regenerative Medicine PhD program
Scientific Director, Regenerative Medicine Center Utrecht

The RESCUE students & their research

From bone regeneration to cardiac repair: a wide range of topics has been covered in the RESCUE research projects. Here, we introduce you to the students and their main focus of study during their PhD.

Madison Ainsworth

Madison's project used biochemical and structural cues using **converged (bio)fabrication technologies to guide 3D tissue regeneration**. She focused on enhancing tissue structure, cell differentiation, and nutrient supply. As such, she combined atmospheric pressure plasma jet treatment and melt electrowritten (MEW) scaffolds, enabling covalent immobilization of biomolecules, like TGFβ1, to guide differentiation of mesenchymal stromal cells. She devised a method to introduce out-of-plane porosity in scaffolds by using a co-MEW technique with a sacrificial sugar-based material, enhancing pore interconnectivity. Finally, she created a patterned myocardial-vascular construct using MEW and extrusion-based bioprinting, to mimic both heart muscle and blood vessels.

Saeed Arbabi

Osteoarthritis is a major cause of disability worldwide. Saeed applied MRI sequencing and spectral CT to **image knee osteoarthritis in order to grace the disease and find early markers** to predict progression. He has worked on a software pipeline for detecting these pathological conditions. This was used to produce quantitative scorings which can help radiologists save time during their diagnosis, improving the accuracy of their diagnosis, and avoiding false negatives in detection. He also developed a deep learning automatic segmentation method that could allow for analysis of conditions like bone erosion in the foot.

Murillo Bernardi

Murillo worked on the **application of kidney organoids derived from adult stem cells (ASC)**. These organoids display transport function similar to native tissue. In his project, Murillo used them in a 3D-printed scaffold for further transplantation and integration in the host vasculature, with the goal of regaining kidney function. In the process, he designed and 3D-printed the scaffold and standardized an assay for in vivo vascularization of the construct, which can be used prior to transplantation.

Thomas Brand

Senescence (biological aging) is involved in the development of many chronic diseases, notably in cancer and fibrosis. In his project, Thomas aimed to better detail **how senescence formation affects pathological progression through induction of stemness** (a property of a cell that allows it to be self-renewing and differentiating), and whether the detrimental effects of this stemness induction can be lessened using senescence-targeting drugs. With a liver organoid model, he replicated and observed the stemness-induction effect of the senescence-associated secreted factors, and evaluated that it impairs the differentiation process of the organoids.

Leonardo Cecotto

Bacterial infections can lead to orthopedic implant-failure. Implant surface modifications could prevent infections. Most preventing strategies aim to kill pathogens approaching the implant. These strategies do not consider the possibility of bacterial invasion of host cells as shelter, while growing and interfering with cell function. In his project, Leonardo **built an in vitro co-culture model that closely mimics the scenario of implant infection**. This model functions as a predicting tool to determine efficiency of preventing treatments against implant-associated infections. The model is used to characterize cell behavior in the presence of intracellular bacteria. He hopes to use the model to better characterize antibacterial properties of a coating involving silver ions. He also used nanogels that release their antibiotic contents intracellularly to target bacteria surviving inside of cells.

Aina Cervera i Barea

Chronic heart failure as a result of ischemic heart disease is a growing epidemic burden with no widely available treatment. In her project, Aina explored **the use of the epicardial cardiogenic factor Follistatin-like 1 (FSTL1) to induce regenerative effects to treat chronic heart failure**. She used human induced pluripotent stem cell-derived cardiomyocytes to investigate the potential cardioprotective and regenerative properties of FSTL1. She also tested the therapeutic potential of FSTL1 in a large animal model. Eventually, the project aims to develop new cures for frequent and serious heart diseases currently treated mainly with symptom relieving therapies.

Nino Chirico

Thanks to advances in tissue engineering, what was considered science fiction ten years ago is now at its primordial state. Although we are still several decades away from of-the-shelf engineered organs, some research groups are moving in that direction. The main aim of Nino's project was to **generate a clinically-relevant size human bioengineered cardiac construct that replicates the native cardiac tissues** from both the cellular and structural perspective. To do so, he replicated the cardiac tissues' native cellular composition and ratios, maturation, cell-cell interactions, and 3D arrangement. He then aimed to match the native tissues' mechanical properties, topographical cues, fibers orientation, and biochemical composition. Finally, he aims to achieve proper functional activity and vascularization in the bioengineerd construct.

Lorenzo Costa

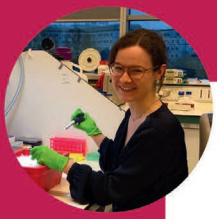
During his PhD, Lorenzo has been working on an analysis to understand **which brace types (rigid full/part time, night time and soft braces) have the best success rates for treating spinal disorders**. To classify the maturation of the spine, he conducted a CT study to understand the pattern of ossification ('bone tissue formation') of the ring apophysis (protuberance of the spinal discs) in vertebral bodies. He then worked on detecting it on MRI scans, which are radiation free. He proceeded to design a brace treatment for spinal muscular atrophy (SMA), and worked on a prospective study on alterations and development of the intervertebral disc in AIS (adolescent idiopathic scoliosis) patients.

Alessandro Cutilli

Allogeneic hematopoietic stem cell transplantation (allo-HSCT) is the most effective therapy available to treat high-risk hematological malignancies and other inherited and acquired disorders. Yet, it is also associated with side effects, most commonly Graft-versus-Host Disease (GVHD), characterized by the reaction of immune cells from the donated material against patient's tissues and organs. Alessandro **developed a 3D model system to study fundamental aspects of T cell behavior in the context of intestinal damage**, with aim to understand better GVHD in a translatable setting. He also studied autophagy in CD4+ T cells, as inhibition of autophagy could be used to induce tolerance in immune disorders characterized by the presence of hyperactive T cells, like in GVHD.

Leanne De Silva

Autologous bone grafting is currently the most widely used method for treating critical-sized mandibular bone defects. However, it often results in donor site morbidity and has limited availability. Leanne's project aims to **improve the clinical translation of endochondral bone regeneration (EBR) for the treatment of mandibular bone defects**. During her project, Leanne studied the use of devitalized allogeneic MSC-derived constructs for EBR, using preclinical models. In order to scale up, creating constructs of clinically relevant size requires vascularization. Leanne's project also explores the use of an arteriovenous (AV) loop model for upscaling in bone tissue engineering. The AV model was used for intrinsic vascularization, which is the natural development of a network of blood vessels originating from a specific, predetermined blood vessel.



Vanessa Disela

After wound closure, cells from the epidermis receive instructions from the underlying undifferentiated tissue, the blastema, in order to form new hair follicle. But how exactly the blastema cells do so is unknown. During her PhD, Vanessa aimed to **identify the epidermal stem cells, which give rise to hair follicle, and uncover the signals by the surrounding tissue**, which instruct them to do so. For this, she has used epidermal organoid culture to induce hair formation in adult stem cell-derived epidermal organoids of African spiny mice in order to study wound-induced hair follicle regeneration. She has also applied single cell RNA sequencing to study skin regeneration at the single-cell level to identify the epidermal stem cells giving rise to hair and their regulation in vivo.

Jie Du

Low back pain (LBP) is a common health problem and a leading cause of disability worldwide. One major cause for low back pain is symptomatic intervertebral disc degeneration (IVDD). To date, alternative treatments are limited. Disc surgery remains the last option when all other strategies have failed, but the outcomes are disappointing. With his project, Jie aimed to **reveal the IVD degeneration processes and propose potential therapeutic routes** to halt degeneration and achieve regeneration. He has developed a model that can be used to further elucidate mechanisms of IVD degeneration. Additionally, he has studied the potential of combined cellular, biomaterial and bioactive approaches for AF regeneration, identified CD146 as a useful marker in AF repair strategies, and explored retention of small molecules for more effective IVD treatments.

Sammy Florczak

Sammy's research leverages expertise in optics and photonics to **innovate in volumetric bioprinting, aiming to advance the development of tissue engineering scaffolds**. The study introduces novel optical configurations that facilitate the creation of smarter and more intricate scaffolds, essential for supporting and nurturing the growth of biological tissues. These configurations are meticulously designed to improve the precision and capabilities of the volumetric printing process, thereby enabling the production of scaffolds that more closely mimic the complex structures found in natural tissues. Furthermore, the research employs advanced imaging techniques to observe the printing process. Together, these innovations in optics, photonics, and imaging contribute to the production of superior-quality tissue engineering scaffolds, paving the way for more successful tissue regeneration and repair applications.

Su Ji Han

Arrhythmogenic cardiomyopathy (ACM) is one of the leading causes of sudden cardiac death in young adults, especially athletes. The main hallmarks of the disease are arrhythmias and progressive fibrofatty replacement of the myocardium, which can ultimately lead to heart failure. While the genetic basis of ACM is well understood, where most of the patients harbour a mutation in desmosomal genes, predominantly in plakophilin-2 (PKP2), the underlying molecular mechanisms that drive the disease largely remain unclear. To further understand ACM pathogenesis, Su Ji used human induced pluripotent stem cells generated from patients carrying a pathogenic mutation in PKP2 and a mouse model that has the human equivalent PKP2 mutation. By performing RNA-sequencing, molecular and functional studies with her in-vitro and in-vivo model, she aimed to **identify new pathways that are involved in ACM and explore new therapeutic targets** to find effective treatments for patients.

Alasdair Irvine

During his PhD, Alasdair identified high-potential, advanced in vitro models. He then developed a validation strategy to ensure their suitability for regulated use and testing. The outcomes of his research have been used to develop guidance documents that provide information on method characteristics and ethical and regulatory aspects. Finally, he collaborated with key stakeholders including regulatory bodies, industry experts, and scientists, to **determine which dissemination strategies are most appropriate to position the in vitro models as alternatives for animal experimentation**.

Paree Khokhani

Using autografts is still a gold standard for treating critical-sized defects and fracture non-unions. Recently, synthetic ceramics have been non-inferior to autografts. Despite this, a 100% fusion rate is still not achieved. In her project, Paree aimed to test a **novel immunomodulatory strategy that could be applied to synthetic ceramics to boost their performance** and eventually enhance bone formation. She tried various commercially available bacterial cell wall components for bone formation using in vitro and in vivo models. She also developed a novel in vitro model considering immune and bone-forming cells.

Aoife Kilgallen

In her project, Aoife aimed to understand the concept of cardio-oncology. She investigated the role of the circadian clock in chemotherapy-induced cardiotoxicity on various cardiomyocyte cell types. Cancer is one of the leading causes of death, with cases expected to rise to 24 million people. Due to improved diagnosis and prognosis, more people than ever are surviving cancer. A portion of these cohort of patients surviving cancer are developing severe secondary adverse effects as a result of being administered chemotherapeutic drugs known to cause cardiotoxicity. Aoife **investigated whether chrono-modulated chemotherapy improves the efficacy of chemotherapy drugs while improving the toxic side effects** experienced by cancer patients. In another project, she has aimed to improve the diagnosis of carcinoid heart disease (CHD) by identifying new possible biomarkers in CHD patient serum.

Dominique Kolly

Hematopoietic stem cells (HSCs) are responsible for all blood cell production throughout life. Defects in HSCs lead to various blood-related disorders and cancers that are in part treated by HSC transplantations. Located in the bone marrow in adult, HSCs are initially produced in the aorta during embryonic development. In her project, Dominique aimed to determine the precise spatial and temporal expression patterns of key regulators in **signalling pathways involved in endothelial specialization and HSC production**. With this knowledge, HSCs could potentially be generated from a surrogate aorta in vitro. The project helps to better understand the molecular events controlling HSC formation in vivo, a pre-requisite to improve the in vitro production of HSCs that are needed to treat patients with blood related disorders.

An international community:

where are our students from?

Tijana Ljubik

Amyotrophic lateral sclerosis (ALS) is a lethal neurodegenerative disease characterized by progressive loss of upper and lower motor neurons, for which no curative treatment is available. Recent studies show that motor neuron death is multifactorial and suggest that the immune system, especially microglia, are involved in disease pathogenesis and progression. Activated microglia are a hallmark of ALS pathology, however their exact role in the pathogenic process underlying ALS remains elusive. Tijana **developed organoids carrying ALS associated genetic defects**, to study the contribution of this gene defects to an altered immunity and neurodegeneration. Her primary goal has been to unravel the roles of the immune system and the cell metabolism in ALS pathophysiology. To this end, she applied "omics" approaches (genomics, transcriptomics, proteomics and metabolomics) to deeply phenotype the ALS-iPSC systems.

Ranganath Maringanti

In his first project, Ranga aimed to **define a complete system to study atherosclerosis on a microfluidic chip**. He incorporated both human-derived endothelial cells and vascular smooth muscle cells to create functional larger vessel surrounded by a 3D extracellular matrix. To mimic atherosclerosis-on-a-chip, he incorporated monocytes under flow, creating plaque in the micro channels and performing functional studies. In his second project, he studied the genetics of chronic kidney disease, focusing on DNA regulatory elements that are located on both protein coding and non-coding regions. Eventually, this may aid in discovering regulatory variants associated with CKD, and unravel mechanisms from the genetic level in order to treat CKD or minimize its progression.

Vuong Tuong Vy Nguyen

During her PhD, Vivian studied kidney related diseases in a **multi-organ-on-a-chip (MOC) model that allows for screening of candidate therapies for kidney regeneration**, hopefully reducing the amount, costs and burden of animal experiments. She aimed to establish an MOC of a renal tubular system with functioning proximal tubule transport that interacts with the liver and other relevant organs. Using this MOC, she modeled acute kidney injury and monitored physiological effects of mesenchymal stem cell (MSC)-derived extracellular vesicles (EV) in kidney regeneration after injury. Additionally, she investigated the systemic effects underlying the regenerative effect of MSC-derived EV in kidney disease.

Clémence Odille

Heart transplantation remains the standard therapy for patients with end stage heart failure. Although heart transplantation is being performed in the clinic for 50 years, the preservation techniques up to 4 hours are still far from optimal. In her project, Clémence aimed to **optimize ex-vivo cardiac perfusion to achieve 3 to 7 days preservation**. To achieve this, she worked with a mouse heart perfusion model, to identify the optimal combination of perfusion temperature and fluid, rewarming strategy, and type of flow. Subsequently, a pig heart perfusion model better reflects human cardiac anatomy and physiology.

Sara de Palma

Neonatal brain injury (NBI) is a leading cause of mortality and neurodevelopmental impairments such as cerebral palsy in term-born infants. Current therapeutic options are very limited. Therapy with mesenchymal stem cells (MSCs) is a new promising strategy to boost neuroregeneration of the injured newborn brain via paracrine signaling. The MSCs secretome may aid recovery of affected neurons and generation of new neurons, oligodendrocytes and astrocytes from endogenous neural stem cells. During her PhD, Sara aims to **optimize the secretome of MSCs by different preconditioning strategies and investigate neuro-regenerative potential of optimized MSCs**. For this purpose she also uses omics techniques, particularly proteomics to characterize secretome of naïve and preconditioned MSCs. Next, she explores migratory routes of MSCs from the nasal cavity to the inured areas of the brain after intranasal administration in animal models of neonatal brain injury, to further validate MSCs therapy for clinical application.

Francesco Palmieri

Francesco's research focused on the **production of a well-defined (chemically and physically) 3D environment that can be used as a cell culture medium**, active scaffold for transplantation or injection of stem cells. In his first project, he developed a robust protocol that allows him to use an automated system for the synthesis of any type of glycan independent of the nature of the substrate itself. In his second project, he produced a library of hydrogels. Using natural and synthetic materials and different types of biocompatible ligation he tested the effects of different chemical and physical properties on stem cell growth, proliferation and differentiation. Finally, he developed novel chemical/chemoenzymatic routes to synthetize biopolymers. In material science, these biopolymers can be used as a primary scaffold in biomaterial production having novel chemophysical properties. In immunology, they can potentially be used to more efficiently produce antibodies and vaccines.

Nada Ristya Rahmani

Nada has been working on the iBone project, **screening immune modulators on their capacity to induce regeneration of bone tissue** in both vitro and vivo setting. To study this, she has conducted a study on rabbits that were either immunized with an immune modultor agonist, or blank. Based on these results, she concluded that the agent did not have opotential to be applied for bone regeneration strategies. In another project, she aimed to investigate the effect of Pathogen Recognition Receptor (PRR) ligands on the differentiation of osteoclast from human monocytes. Literature suggests that osteoclast are required in material-induced bone formation. The results showed that monocyte-derived osteoclast differentiation was hampered PRR ligands that stimulated higher pro-inflammatory cytokine production by monocytes.

Laura Serini

In her project, Laura addressed the challenge of **developing protein degraders for cancer therapy in the context of Targeted Protein Degradation**. Conventional treatments, using monoclonal antibodies or small molecule inhibitors, have limitations in terms of side effects and resistance. The project aimed to develop an innovative technology named SureTACs (Surface removal Targeting Chimeras) to selectively target undesired cancer proteins for degradation. She identified target proteins, set up a novel screening platform and, to study this further, she made use of tumor cell lines and organoid-based model systems.

Jui Anil Shinde

The goal of Jui's project has been to **understand the maintenance of cell polarity in healthy and disease conditions**. She studied this by investigating the role of recycling endosomes and CHEVI complex in maintaining cell polarity in kidney & liver polarised epithelial cells. The CHEVI complex is important for the polarised trafficking of various proteins from recycling endosomes. Mutations in genes of the CHEVI complex cause the severe multi-system disorder ARC syndrome (Arthrogryposis, renal dysfunction & Cholestasis), displaying loss of polarity in the epithelial cells of bile canaliculi in liver and of the proximal tubular cells in kidney nephron. Jui has been interested in understanding the role of CHEVI in recycling and identifying the cargo protein that depend on CHEVI for their trafficking.

Zahra Shojaeijeshvaghani

Many patients with very early onset inflammatory bowel disease (VEOIBD) do not respond to conventional treatments. To **identify novel therapeutic drug targets and guide the clinical decisions in a personalized way**, Zahra established a living biobank of ~150 pediatric IBD patient-derived organoids from different locations in the gastrointestinal tract. She generated a transcriptomics dataset for each patient, to study microbial responsiveness and identify patient-specific perturbations to predict possible therapeutic interventions. Additionally, she developed functional assays on organoids to identify intestinal epithelial phenotypes resulting from known gene defects in VEOIBD patients. In the future, these organoids will be used for screening therapeutic compounds in a patient-specific manner.

Neha Singh

In her project, Neha focused on **developing stem cell therapy for the treatment of hypoxic-ischemic brain injury in neonates**. She aimed to investigate the molecular and physiological impact of intranasal stem cell treatment in murine models of hypoxic-ischemic brain injury. Furthermore, Neha studied functional recovery of neuronal networks after stem cell therapy by in vivo behavioral paradigms as well as ex vivo electrophysiological assessments.

Laura Varela Pinzon

Cell-derived extracellular vesicles (EVs) are present in synovial fluid and cartilage extracellular matrix, and thought to be involved in joint development and in the regulation of joint homeostasis. In her research, Laura aimed to **identify and characterize EV subsets isolated from synovial fluid** from both healthy and disease equine patients, and from human patients that developed inflammatory articular disease. She then characterized (functionally) and correlated equine stem cell-derived EVs with EVs present in healthy joint derived synovial fluid.

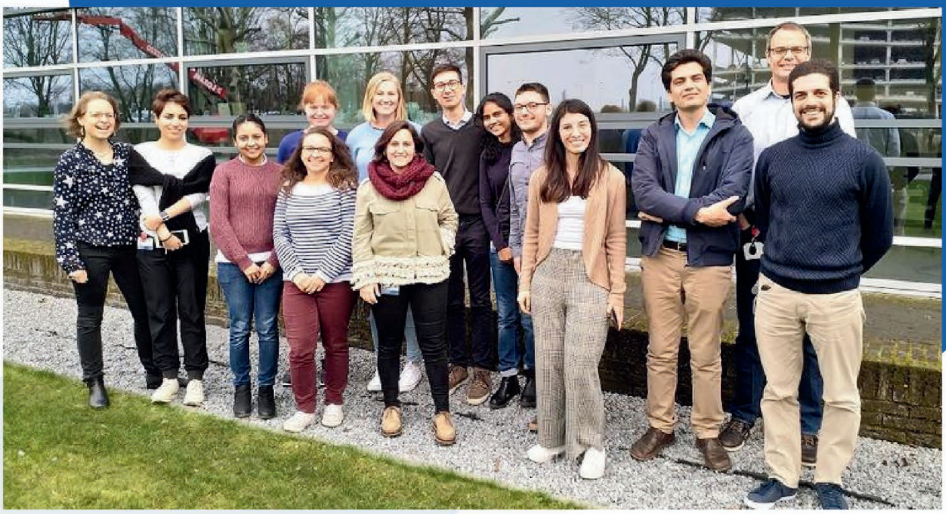
Martina Viola

During her PhD, Martina focused on tissue engineering, with the goal of **combining innovative natural and synthetic materials and biofrabrication techniques for cartilage regeneration**. She used techniques such as Melt Electrowriting: producing fibrous 3D structures from fused polymers through controlled deposition of nano- and micro-fibres. She combined different materials to create a scaffold that manages to reproduce the internal structure of the cartilage. This includes reproducing the conformation that the cartilage takes near and far from the bone tissue, and the mechanical properties it has in different areas.

RESCUE: an international community

"Socially, the RESCUE program was amazing. We were all internationals coming here to Utrecht and for most of us it was the first time. We didn't know anyone and were new to the country. And then you find yourself in a room with all new people who are in the same situation as you are. That was a really good starting point for making friendships."

"When I got here, everything was new and I got this opportunity to talk to people from different countries in Europe and Asia, which was really cool. And because it was an international program, you didn't see yourself as an outlier, because nobody was Dutch. I think that was cool."



"I do think that if I wasn't in the RESCUE program, finding friends would have been harder. So I think that made it easier to move. It puts you in an environment where you can meet people that are in the same situation as you, who also just moved and are also looking for friends. It was a bit lonely in the beginning, which is normal, but then I quickly made some friends here."

"It was nice to start as a group. The transition to living a normal life here was a bit difficult because we were supposed to hand in and take care of a lot of bureaucracy that we weren't really prepared for. But I got to meet lots of people and we created our own social network. It's nice to know there's a bunch of people who started around the same time and feel just as lost as you are, and that you can lean on."

"We were all new to the Dutch system and research and the struggles of a PhD, so you always had a safety net. We shared the struggles, especially bureaucracy and paperwork. We really helped each other out with that."

"There was good bonding between us and we found a lot of support with each other. Especially if I had a personal problem, or something work-related, I'd ask the other RESCUE people."

Life in the Netherlands

Moving to a new country brings along challenges and culture shocks. How have the students experienced their time in the Netherlands, and which aspects of work and social life here in Utrecht have surprised them the most?

At work

(Lack of) formality

- "I like that here **your boss is more just like a colleague**. It leaves more room to express yourself."
- "There's **less of a power struggle** here with supervisors. You're also **expected to be more upfront** with your thoughts, but it's ingrained into my brain to not contradict my supervisor."
- "It's cool that **there isn't really a hierarchy**. My supervisor told me to call them by their first name. I really couldn't at first."

Social

Speaking English

- "I like that **everyone speaks English** here, so you can communicate with everyone."
- "Socializing was more difficult outside of work. When people realized they had to speak English, **they'd back out sometimes**."
- "The **language barrier** that you experience in many other places wasn't really a thing here."
- "In situations where most people were Dutch, they'd sometimes only **speak Dutch with each other**."

Intercultural communication

- "Dutch people **interrupt each other all the time**, which is impolite where I'm from. So initially I would just sit there, waiting for my turn to speak, and it would never come. People would think I'm shy, which I'm not. I learned to speak up eventually."
- "The environment we work in as PhD students is not the most relaxed, and you also have to be able to **communicate with people from different cultures**. But if that other person doesn't understand the intercultural communication issue, **they might think it's a personal issue**. That can be tricky."
- "People show emotions less here, and when do you show them in a work environment you **can come across as unprofessional**, like you're letting personal circumstances get in the way of reaching your goals. Which I don't think is true at all. It's **important to be able to show your emotions**, because at the end of the day we are working with people."

Making friends

- "Where I'm from, you can meet someone and immediately connect and talk and say: that's my friend. Here, **'colleagues' and 'friends' have very specific definitions**, and they don't easily mix."
- "**Dutch people are patient**. They take their time to listen to you, do something for you."
- "People here are not as immediately friendly. **Meeting random people is not as easy** here, it's more normal to sit down at a bar with your friends."
- "Dutch people are **friendly in different ways**, they're less touchy and affectionate than where I'm from. I integrated easily though, I felt that people were very welcoming."
- "It **takes effort to make friends with Dutch people**. And when you do arrange a dinner or something, they can usually only meet up in like two months."
- "The Dutch society is pretty **individualistic**. I'm very used to being in a social community, so coming here and becoming individualistic can quickly become lonely."

"There were some things I missed about home, but the nice thing is that it made going back to where I'm from even better."

Meetings and supervision

- "I come from a culture where you tend to be more supervised, and be told more or less what to do. Here, **you're expected to be more independent**."
- "I **didn't get as much feedback** during meetings as I was used to, so I wasn't sure if I was doing things right or not."
- "You're expected to **actively ask for meetings**, which can be difficult."
- "The amount of meetings you have was shocking, I had **so many meetings**. At one point I was doing more bureaucratic things than lab work."

An organized culture

- "The Dutch **schedule everything**. It's difficult to do spontaneous things. It only happens when everyone already took time off with the idea to 'see what happens'."
- "I **love how organized and arranged everything was** here. There were so many people to help me figure things out."
- "I **appreciate how calm Dutch culture is**. The people are not busy all the time and the city is not as chaotic as where I'm from."

Cycling

- "**You bike so much**! That might be the standard cultural difference everyone notices, but it still shocked me when I got here."
- "I think **the bike culture here is very cool**. You can just take your bike and go anywhere."
- "I do really enjoy the cycle lanes, and the sidewalks along the canals. That reminds me of home. It's very **calming and relaxing**."

"I like that there's less pressure here than where I'm from, and there's more freedom."

Collaboration

- "Collaboration is a big thing here. There is **a lot of teamwork** and people giving their opinions before making a decision."
- "There are a lot of **experienced people** around, and it's good to learn and take suggestions from them."

Dutch directness

- "The Dutch are **very direct** and it doesn't always feel good to hear. It's efficient though, and you need to see it as a form of attention and wanting to **help you move forward**."
- "I did have a lot of difficulty with the Dutch directness. Where I'm from that would be considered completely rude, and here it's seen as efficient. It's a **different mindset**."
- "I **appreciate the clear feedback** here, the direct communication. It results in faster progress and leaves no room to be interpreted differently by others."

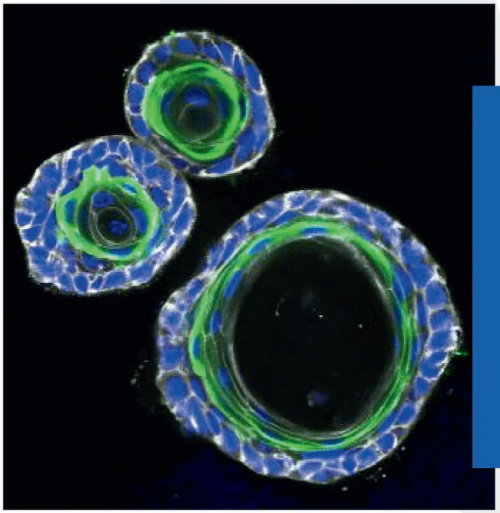
Food

- "Our **food tradition is quite different**, but I'm glad I can still buy a lot of things I'm used to at markets. That's **comforting**."
- "I do **miss good food**. Usually I cook myself food to take with me, but it takes a lot of time."
- "People **don't eat hot meals** for lunch, which I do like to do, so I just bring my own food."
- "Where I'm from we have many nice desserts, which I miss. And **eating out is cheaper** there."

- "I had to get used to the Dutch honesty. If they don't like something, they will immediately tell you. And I think now I **see it as an advantage** because at least they don't tiptoe around it. But it can be quite confronting."
- "Dutch people are very direct. They are **honest and straightforward**. I am not used to that, so initially that sometimes came across as rude to me. That was something I really had to get used to."

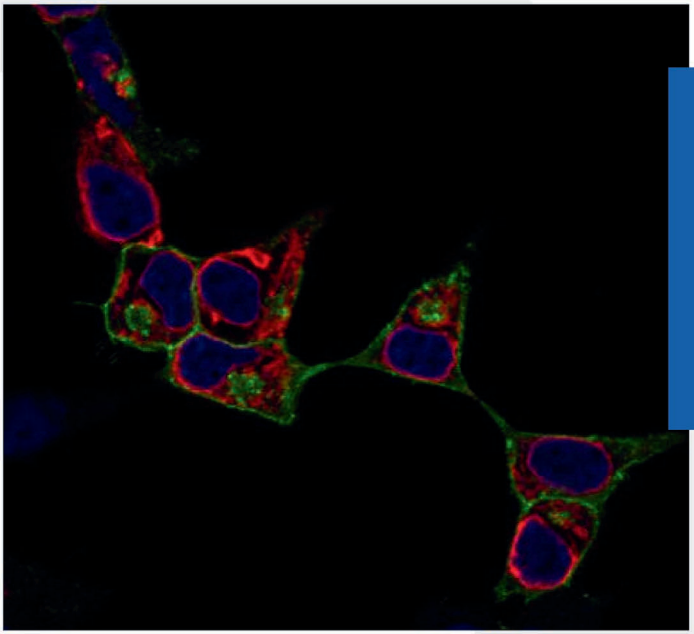
Sammy Florczak

"Here I am, working on the volumetric printer I designed and built on an optics table. The device is an advanced 3D printing technique capable of fabricating structures of any complexity within a matter of seconds. It uses lasers and spatial light modulation to project a series of tomographic projections into a rotating vial filled with a photo-crosslinkable resin. The sum of the projections creates a 3d light dosage distribution within the resin, thus causing it to solidify to any desired geometry."



Vanessa Disela

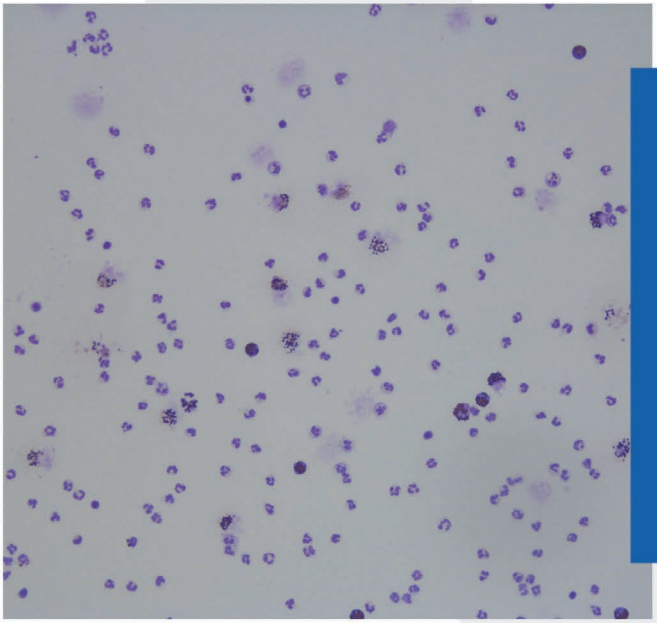
"This is a confocal image of the Spiny mouse epidermal skin organoids with inside-out morphology I generated.
Blue labels the nuclei (DAPI), white abels actin (= cytoskeleton of the cells) and green labels a cytokeratin, which labels the cells on the outside of the skin."



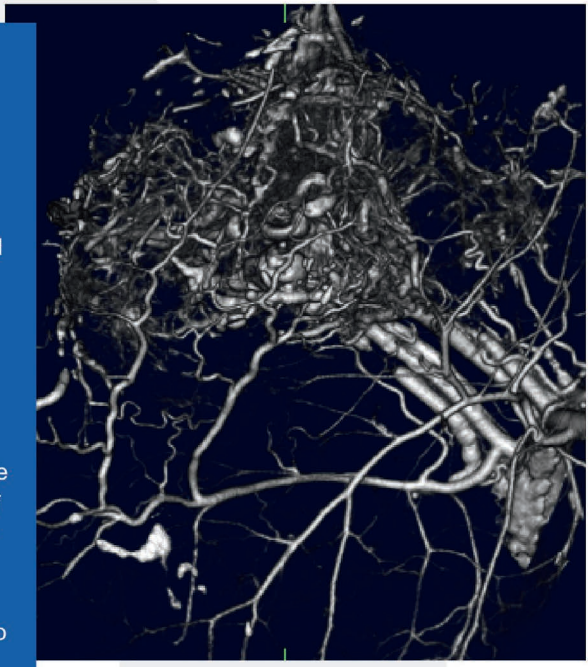
Laura Serini
"Here you see a microscopy picture where we characterized a membrane-bound E3 ubiquitin ligase, which so far has been insufficiently explored."

Lorenzo Costa
"Here I and a student (Mohammad Mansour) developed a software to make a brace for patients with Spinal Muscular Atrophy in need for spine correction and pain relief."

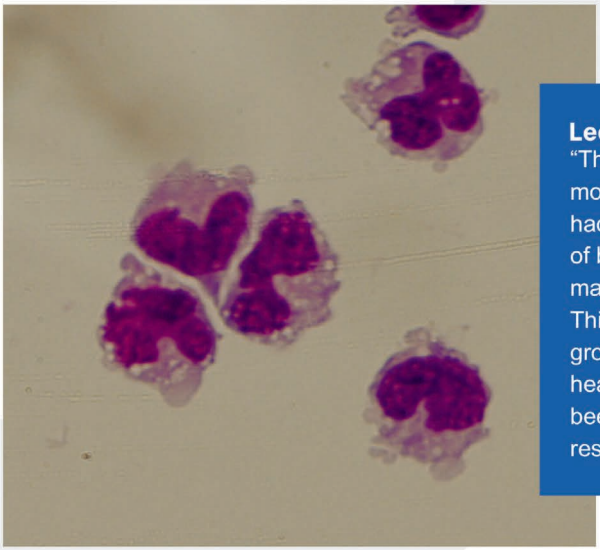
Aina Cervera i Barea
"In this image I am petting the pig right before I conduct the live read-outs of its pacemaker. In my line of research, it is of the utmost importance to ensure the adequate wellbeing of the animals while we conduct this type of experiments. We do not want to add any more stressors than the disease they are already carrying and so ensuring they are well taken care of and getting them to know the researchers behind the interventions it enables an accurate acquisition of data."



Laura Varela Pinzon
"Here you see a Wright-Giemsa stain for differentiation on the morphology of blood cell types. Equine neutrophils were isolated from the blood of healthy donors and stained with Wright-Giemsa. The picture depicts the isolated neutrophils and some co-isolated basophils."



Leanne De Silva
"The AV loop project has undoubtedly been the most challenging part of my PhD. You can do everything right, have the head of maxillofacial surgery join you in surgery and still have a non-patent loop. Which, btw you only find out after a gazillion hours of surgery and at the end of the experiment. So this is a microCT image of a patent loop after 4 weeks and to make it inspirational, it is a symbol of remaining resilient during your PhD, because you can plan and do everything right, and everything will inevitably still go wrong. Yet in the end, everything will come together because it has to."



Leonardo Cecotto
"This picture belongs to one of my most boring experiments where I had to manually count the number of bacteria phagocytosed by macrophages and neutrophils. This is the image from the control group without bacteria. I found a heart-shaped macrophage. It has been in every presentation of my results ever since."

How to: get through a PhD?

Why is it important to go out of your comfort zone every now and then as a PhD student? And how do you look after yourself in the midst of the stress? From their personal experiences, the RESCUE students give advice on finding a PhD position that suits you, and how to make the most of it.

"Don't just accept any PhD position that comes to you; be critical"

- "Before you start, **make sure the group is generally happy** with their supervision and that there's enough guidance for them to thrive, learn and be able to make mistakes but not be alone in carrying the consequences."

- "I didn't do any research regarding the lab or the people working there, which I think was a mistake. **Make sure you can talk to the people in the lab**, do a lab visit if you can. Know what you can expect from the people around you. Talk to other people as well, aside from just your supervisors and your PI, like people who have just finished their PhD in that lab. **Check what their experiences are or have been**, and how their project is going."

- "Don't just accept any PhD position. Before you start, **look at the size of the group**. If it's big, you know it's probably set up well and you'll find more support and feedback. If it's small, look at the PI and figure out how they work. Check if they still work in the lab, and if they'll be working with you."

- "Make sure you're **interested and content in the field** that you'll be working in first. Then go on multiple lab interviews and get a feeling of the PI and the other people. Look for a lab with people that you click with."

"Be open to learning new ways of communication"

- "Learn how to communicate with your supervisor. Where I'm from, I learned that you should never interrupt your supervisor. Here, they don't even let you finish a sentence in the meeting. So it's very **different perspectives**."

- "I would advise anyone to read the book The Culture Map. It really showed me that some of the **communication issues** I see between colleagues are not a personality thing, but rather a style of speaking. And for internationals: **be open and communicate your thoughts**. Many things are new to you, so share what you observe and someone might be able to explain these things."

"Go out of your comfort zone at times to get new experiences"

- "Go a little **out of your comfort zone** every now and then. Go abroad, improve your English, improve your skills, meet other people that don't think exactly like you do. I think that would be beneficial to anyone."
- "I had a lot of support from my friends because we all were in the in the same boat. For me that was really nice, as **I saw a personal growth in me** because of this experience, and that was a new thing. You can't get this kind of experience anywhere else."
- "I'd recommend to **experience some of your time abroad**, which doesn't mean that you have to move permanently. But I think it can help, and it's a nice opportunity to push you out of your comfort zone a bit."
- "If you can, **work in a different lab or at a company for a while** during your PhD. It was the most productive time of my PhD, and it brought back my motivation completely. Working at a company let me see a different environment and work with different people."

"Make sure there is a plan for your project before you start"

- "Ask for a **full protocol at the start** of your project. I think it's important to have a clear aim and overview of what your PhD is going to be. Of course that can change over time, but that overview is essential."
- "Define your chapters and the research questions for each chapter early in the beginning, and **know where in that plan you can make changes or redirect**. Most of the time it's not possible to fulfil all of these chapters, but at least you know what you want and you can try to find solutions for that."
- "I'd recommend starting your PhD with having a clear idea of: what should I do from a scientific perspective, and also experiment-wise? Design your project from scratch, so that you **have something that can guide you towards your goal**."
- "I saw that **a lot of things don't go as planned**, and it made me feel out of place a lot of the time. So discuss these things with your supervisor to make sure you know what to do **when things don't work out**."

"A PhD can be lonely and demanding, so protect yourself"

- "Try to balance the work environment with your own ambition and expectations from your group. **Balance science and mental healthcare**. In the long term, this will have a very big effect on many aspects of your life."

- "If you feel too much pressure, change groups as soon as you can. Be aware of the environment you are starting a PhD in. And especially in the beginning, **you can still change groups**. After a year or two that's harder, it can feel like you're wasting your time. But even then, you're really not."

- "A PhD can be lonely and demanding. A lot will be expected from you and it's a highly competitive field. **Sometimes it can be too much**. The workload is excessive and you might feel like you're not being productive enough. So make use of all the tools you have to really **protect yourself**. Go to a psychologist from the university, and go to your peers for support so you can share your experience and feel less alone. **Find ways to blow off steam** to not lose yourself in your work. Be okay with setting boundaries, and know you can always report things to HR."

- "**Learn to say no to your supervisors**. Whether it's about a project that you're sure is not going anywhere or if its doing extra things for them that do not benefit you in finishing your PhD, it's important to set boundaries."

- "Realise that **a PhD is something that you do on your own**. There might not be as much teamwork as you expect, and you can feel very strongly that you have the whole project leaning on you. Sometimes you'll just have to figure things out on your own. It can be a nice way to be challenged, but to feel that constantly for so many years can be too much. Try to look for a way to balance that."

- "**Don't compare yourself to others.** They might seem like they have everything together, but they really don't. And comparing yourself to them will only make you feel worse about your own project."

- "Be patient with yourself. **Try to be a friend to yourself**, because it's easy to be hard on yourself, but I learned that I'm harder on myself than I would be on other people. Be kind to yourself. The pressure is already so high."

- "Try to enjoy it! It is very stressful at times. We have this joke that everybody will go through the 'valley of death' at some point, usually in their 3rd or 4th year. **Be gentle, and try to find ways to enjoy it**. I sometimes go around the lab and tell people 'it's okay, you're doing okay, don't be too sad'."

"It's all about expectation management"

- "It's all about expectation management. Not only yours, but your supervisor's as well. So you need to **be flexible** about it too. Let your own plans or expectations go at times. You'll realise everything will work out at the end."

- "In the beginning you and your supervisor will have to get used to each other. You don't know each other well, so you have to **figure out each other's expectations** to find a middle ground."

- "Realise that a PhD is a lot of work, and you'll realise that especially towards the end. And at the same time, **your motivation will not always stay the same**, it's normal if it is high at first but then goes down after a while."

"Bad results are not actually bad; it's just not what you expected"

- "Don't stress about things you cannot control. Biology does what it's meant to do. **Negative results are still results**."

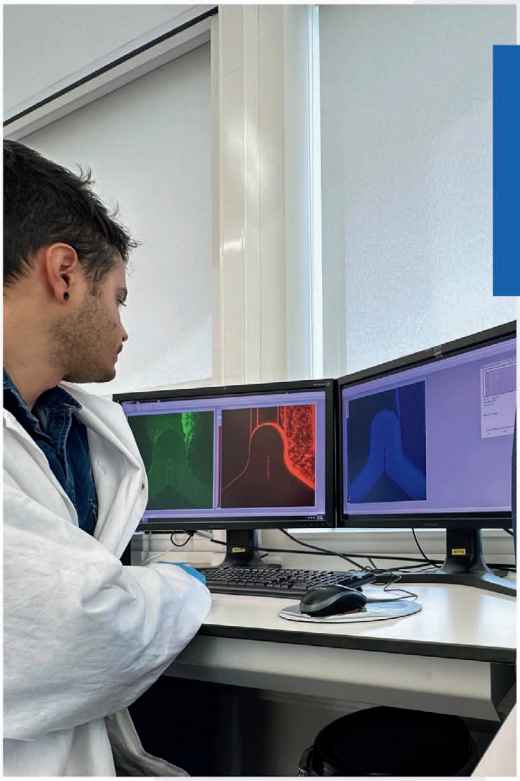
- "Be flexible. You gradually learn that no matter what happens, **it's going to be okay at the end**."

- "In the beginning, **allow yourself to try things** and get some experience, and when you find something interesting, explore that. Of course if you get bad results you'll be disappointed, but a bad result is also a result. And it's not actually bad, it's just not what you expected. **Errors will only give you new ideas or experience**, which help you move forward. It's better to explore and get the 'defeats' at the beginning rather than at the end stage."

"Enjoy the PhD, but also think about what comes after"

- "Try to get an idea of what you can expect from life after your PhD. Where could you stand in five years after finishing up? Think about the possibilities, and what you would like to do. **Explore your personal interests**."

- "While it's good to enjoy your PhD, **try to think ahead sometimes** about what you would like to do after. Look around, get some inspiration along the way and try to keep a focus on what comes after."

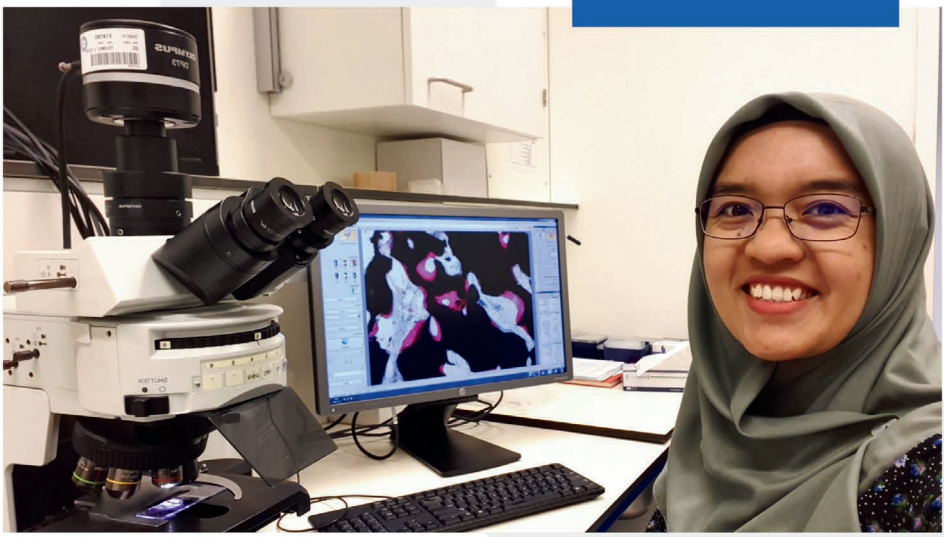


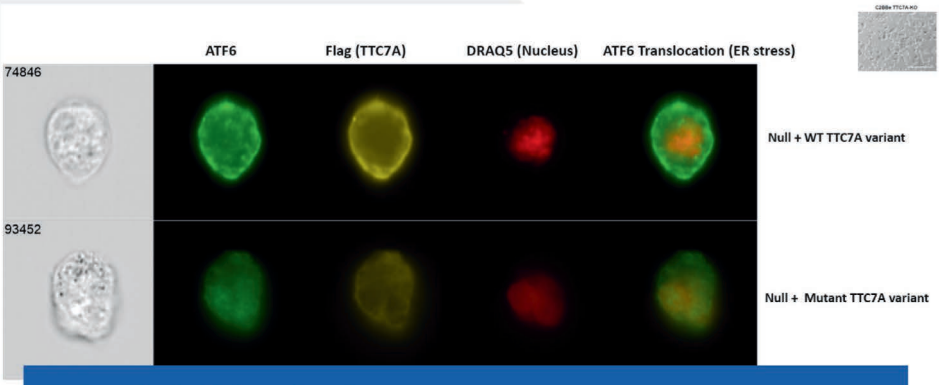
Murillo Bernardi

"This picture was taken at Mimetas during my secondment, where I'm analyzing an immunofluorescent staining of my kidney organoids-on-a-chip."

Nada Rahmani

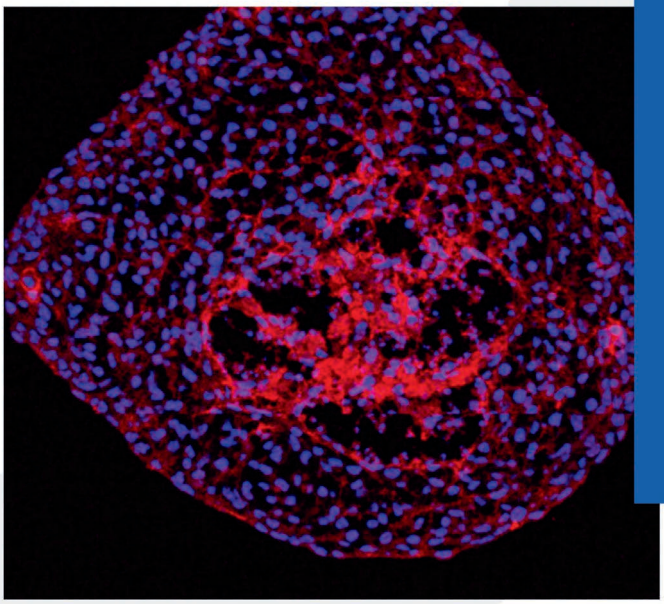
"Here I am, observing the formation of new bone tissue (purple-pink) in the pores of biphasic calcium phosphate ceramics implanted in vivo."





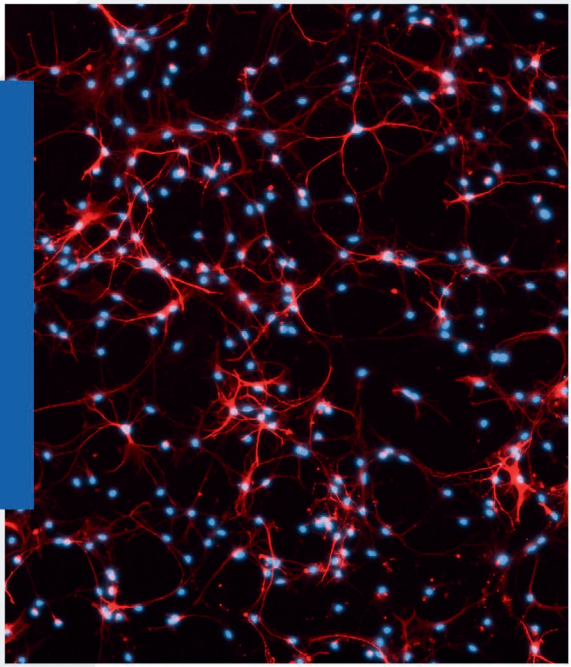
Zahra Shojaeijshvaghani

"These images show C2BBe TTC7A-KO cells expressing either wild-type (WT) (top) or Mutant (Down) Flag-tagged variant of TTC7A. WT TTC7A localizes mainly at the plasma membrane while the mutant variant is more scattered in the cytoplasm. In contrast to cells expressing the WT variant, the cells expressing the mutant variant show increased translocation of ATF6 to the nucleus, suggesting heightened endoplasmic reticulum (ER) stress in the affected cells."



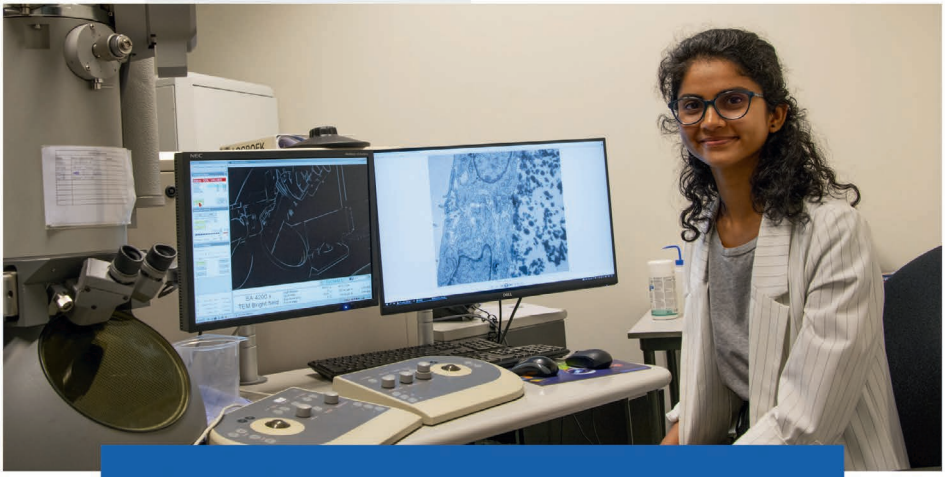
Thomas Brand

"This image shows an iPSC-derived liver bud (3D cellular structure), which has been physically damaged with a syringe, in order to simulate the liver's damage response to partial hepatectomy. The red staining is CD44, which is a stemness marker we are particularly interested in."



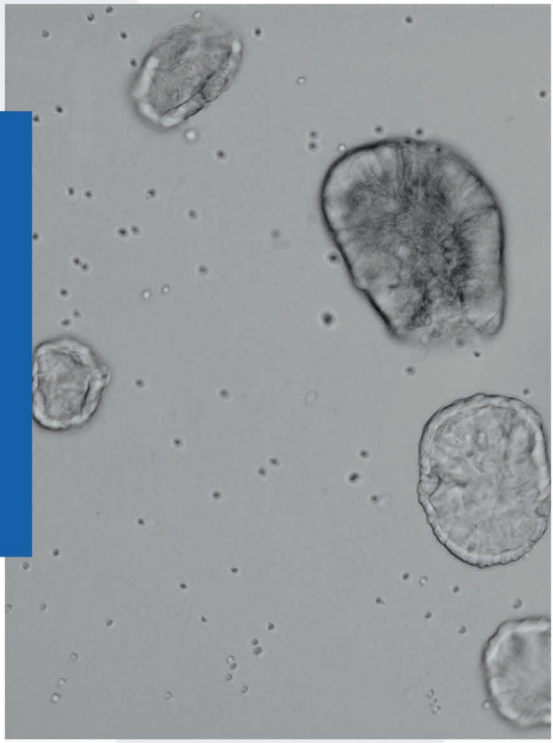
Sara De Palma

"This is a microscope picture of murine neural stem cells differentiated into neurons (red cells, stained for beta-III-tubulin a maker for immature neurons) after a non-contact co-culture with human umbilical cord derived mesenchymal stem cells. In blue is a DAPI staining, so this just marks the cell nuclei."



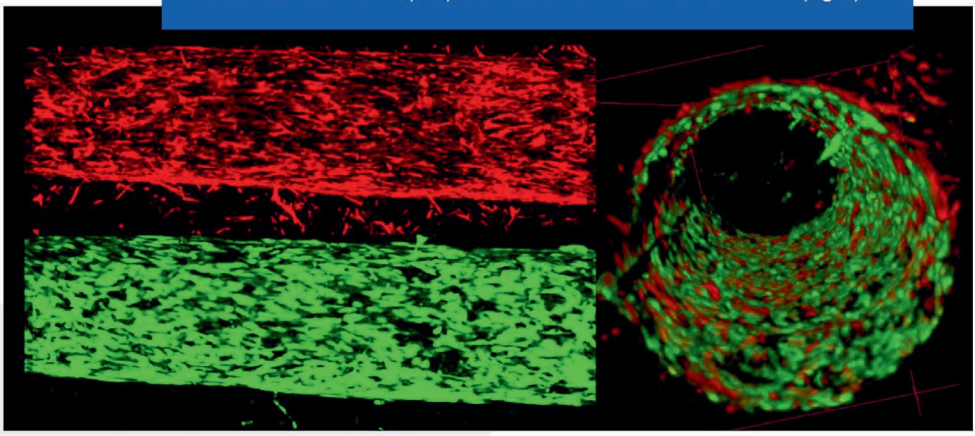
Jui Anil Shinde

"I am using an electron microscope for my research about the alterations of intracellular organelles in healthy and diseased cells. On the computer screen, we can see the ultrastructural morphology of the polarised kidney cells under the microscope."



Alessandro Cutilli
"I model the interaction between the (damaged) healthy intestinal epithelium and immune cells. In this picture, you can see a co-culture in which both intestinal organoids (big structures) and T cells (cells around them) are cultured together in a 3D matrix to study T cell behavior."

Ranganath Maringanti
"Human blood vessel development in 3D-microfluidic system after 4 days. Confocal max. projections of ds-red-h-AoSMCs and GFP-HUVECs (left) and 3D view of the blood vessel (right)."



Mastering mentorship: How to

As a supervisor of a PhD student, how do you best facilitate their research, communicate effectively, and create a comfortable work environment? Drawing from their personal experiences, the RESCUE students offer advice to supervisors and other guides on how to achieve this.

Support in research

"**Science has changed** in the last decades. It keeps becoming more difficult to publish in important journals, because you are asked to use state-of-the-art techniques and methods to prove your point. It's just good to realise that **one person cannot do everything**, and for them to put themselves in your shoes a bit more. The expectations are kept the same, but it's way more difficult to get there."

"Be more attentive to your students, especially in the beginning, **check in on them** more often and don't expect them to know everything that they're doing. **Guide them step by step in the beginning**, tell them what to do next."

"I felt a lot of **pressure to publish**. To me, the focus seemed to be on publishing rather than learning, and I didn't feel like I had enough time to get it all done."

"I would have liked to **collaborate with other researchers** more, and I think that could have been facilitated by my PIs. I would have appreciated help with that."

It's a team effort

"It was **never only about work**, but also having fun outside of the lab. Our group is very close and I think that's definitely because of my supervisor."

"Positive reinforcements and celebrating small wins are imperative to keep up morale. And **a good team fosters good productivity**."

"Don't take **more people than you can handle** in your team."

guide a PhD student?

Personal support

"I'd recommend for supervisors to **talk to PhD students on a personal level**, not only on the basis of work. Rather than starting the meetings asking: 'did you do this', ask and try to get a bit more involved in their personal lives as well."

"Supervisors are experienced, so they know that in the end everything will be okay, but we don't know that yet. So I think it's really important to communicate it again and again: '**it's going to be fine**'. Sometimes that reminder is all you need."

"I'd sometimes receive emails from my supervisor at 3:00 AM, but I knew they **never expected me to do the same**. So I didn't feel pressured to answer, which was good. I was never asked why I didn't check my email during my holidays."

"I was **never pressured into working too much**, which was good. I was always encouraged to go on holidays, which I didn't end up making a lot of use of, but it was nice not to feel that pressure."

"I would have liked **more guidance**. I know a lot of PIs are very busy, and that it can be difficult to mentally put yourself in your student's shoes again, trying to understand the struggle of doing a PhD. But I would have appreciate more support during the project, rather than feeling like I was being left on my own. I would have liked to **feel like there was someone I could ask questions**, and to feel more understood when I was having a hard time."

"It's important to sometimes pause and think: 'in which phase of their PhD is my student right now and **what would be good for their development** at this point?' And talk to them about that."

"The biggest toll you pay for a PhD is mental health. I think it's important to **set up a system that can protect PhD students** from that. And it would be good to organize an information session on how to report things like misbehaviour."

"During Covid, every now and then we were asked to reach out if we had a problem, but **sometimes you're not aware that you're not in a good situation**, or you're not ready to actively reach out yourself. Especially if you're not someone who opens up easily. So I would have appreciated if someone had actively approached me instead, to check up on me."

Effective communication

"The biggest issues came from differences in cultures. Communication between PI's and students can be difficult, and it's always important to take into account that the person you're talking to is from a **different country and background**. That would even help with getting better quality research and a better project."

"It's important for supervisors to take into account that **expats need some time to get used to a new country**. The new regulations, even the language, the way people are. It can be rough, when you're made to feel like you're not good enough or don't take enough initiative. But when we talked about, **it was really just a cultural barrier**, not something that had to do with skills, abilities or motivation."

"More communication among PIs could help develop a well-defined project, and also to have **direct communication rather than through the student**, which held me back in my PhD and research-wise."

"I appreciate my PI **keeping track of everyone** and **being involved** with all of our projects."

"My supervisor is a very **easy person to talk to**."

"We always **discussed together** when decisions needed to be made. My supervisor had the final say, of course, but **I got independence and influence** in that too, which I liked."

"My supervisor is really nice, always wording criticism in a way to make sure you know it's not an attack. He **always makes time for every student**, is on top of everything that's going on, and you **can always talk to him**. He's respectful of my ideas, never dismissive. He'll give suggestions and is **very encouraging of ideas** that you want to explore."

"Some of the **communication went through us, as the students**. It would have been easier if it had been more directly to the PIs. That way we wouldn't have had to tell our bosses what we were supposed to do."

"At times the advice from people from the programme **didn't align** with the advice from the supervisors or PIs, which was confusing."

Meetings and feedback

"It's nice to have sparring sessions and be able to bounce ideas back and forth, especially with someone higher up. Supervisors should **be present and give feedback**. Not feeling productive enough can go hand in hand with not having the best supervision, because you're unsure if you're doing it right or not."

"I like to **only have meetings when I need help**. So only when I got results, or after a month so I could give a little summary. I'm quite independent and I'm glad my supervisor gave me a lot of freedom. **Frequent or fixed meetings would have made me nervous**; I'd always want to have something to show."

"We have regular meetings, which was nice for me. I knew I **could always knock on the door** and ask my questions."

"I **like my weekly meetings** with my supervisor to give an update and they'll give me some structure if I need it, or advice on how to handle certain problems."

Planning and expectation management

"Be **as clear as possible** about the expectations that you have. What's the goal of the project? What's your theory? Which experiments are needed to prove it?

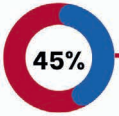
"It helps to **be very practical** and to say which chapters you would put in the thesis right from the start, and how you'd work towards them. It's good to have something to build towards, not having to scrunch something together at the end."

"Take the project seriously, **without being unrealistically optimistic**. I wish my supervisor had been more strict, preventing me from wasting time."

"I appreciated the career events and PhD days, because it helped getting to see people working in the industry or doing a government job. It **broadened my perspective** and helped me to think about where I see myself in the future."

A look ahead: future perspectives

What do the PhD students want to do after their defence? Most are still unsure, leaving multiple options open, awaiting the opportunities:



of the students consider **staying in academia**

Sammy Florczak

"I would like to **do a postdoc**. If I could find an environment like what I have here but in Brisbane, that would be amazing. But if I'm offered a very nice job outside of academia that still offers me a **similar level of creativity and fulfilment**, then I could also consider working outside of academia.

The idea is to go back to Australia. I've been away for so long, and I do miss it, so it would be nice to go back."

"I look back fondly on the conferences: exploring new places, the parties were fun, especially when there were many other people from the lab. And I made friends that I still see regularly."

Thomas Brand

"I think I want to go for a postdoc, but I don't think I want to become a professor. **I would like to be a PI**. Then again, I've never met a PI that's also relaxed and not very intense about their work. Which is not something I want for myself. I like research and the process of it, but **I also want other things besides it**. So I might want to work somewhere where the pressure is lower and I won't have to look for my own money. That might take the edge off."

"Everything is really coming together now and it's shaping up nicely. These years haven't always been easy, but I'm proud of what came out of it. And aside from that, I'm grateful for the people I met."

Francesco Palmieri

"I like the idea of an academic career. **I like the freedom.** I don't like a lot of other aspects of academia though. So many things take away from the actual research. So I'm not set on anything, it depends on the opportunities.

My current options are outside of the Netherlands. It **doesn't really matter where I am as long as it is in Europe**. I prefer Europe, it's a bit closer to my family."

"I've been very happy with my professor and my group. I got to improve my skills and meet many people. I grew up a lot."

Jui Anil Shinde

"I might want to do a postdoc, but it has to be about something that interests me and offers me specific things. **I would want a well-defined project** and know what I'm in for, and to learn a new technique as well. But I'm also exploring other options, like consultancy, which came up through alumni talks and meetups. There are also other types of jobs that I would like, but I don't have the language proficiency for. **I'll have to explore a bit more** and talk to people who are currently doing these jobs, to see what my options are and if I like them."

"I am really happy with the state-of-art facilities that we have here. I got to learn new techniques and play with all these tools, and do my research without any restrictions most of the time. I was really happy with that!"

Leanne De Silva

"Until my defence, I will be working on my thesis and helping out with RM education. After I am done, I am keen on **pursuing a postdoc to remain in academia**. I guess that has always been the plan, but at the same time I am open to anything because I have three fur-children who rely on me having a salary."

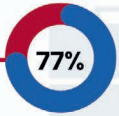
Tijana Ljubik

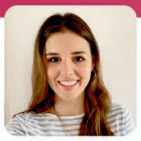
"I want to go for a postdoc right now, but I am **leaving the options open**.

I have a nice established life here, but **most likely I will move because of work**. If I do decide to go into the industry I would probably be staying here."

"The social aspect of the programme has been a real highlight for me. I loved events where we could share our experiences with others. I felt like we were being taken care of. There was always someone I could go to if I had issues."

of the students consider **a job in industry**





Martina Viola

"After my PhD I will **first take a few months off to rest**, and then lookfor jobs either in a company, the industry, or in a research centre. I have some ideas like that.

I'm moving to Germany, and look for a job there or in Switzerland."

"I can't wait to defend my thesis and go on holiday after. It's been a difficult four years, so I'm excited to submit my thesis and wrap it up."

Paree Khokhani

"I want to go into the industry, something related to quality assurance for medical devices. **My PhD made me a biologist**, but really I'm a biomedical engineer.

I am moving to Germany, to my partner. So I'm looking for jobs there."

"My highlight is my personal growth. The first two years were difficult, but I got through it and it's been so much better from there. I learned many soft skills and I think I'm a better researcher now. And I made really nice friends here!"

Ranganath Maringanti

"I want to go for a post doc, but in a company. **Preferably with organ on chip technologies** as well. If that doesn't work out I'd want to work as a research analyst or something like that and do a post doc in academia.

I'll stay in the Netherlands for a while, go for my permanent residence. But it depends on the opportunities."

"Initially, I felt quite lost, but then my project got going. I gained interest in the project and now I've been working on something fascinating for three years. I'm positive about where I'll go after this."

Murillo Bernardi

"I would like to do research in a company. I think things would be **faster and more straightforward**. But in a couple of years, I see myself in more of a manager position. **I like having the bigger picture**, setting goals and thinking about scientific questions, rather than doing the experiments.

I struggle with the winters here. So eventually I might move to a sunnier country."

"I've grown a lot, I'm a totally different person now. This whole experience made me a better researcher and changed my personal life for the better."

Leonardo Cecotto

"I would like to find a job at a company or in the industry and see what it's like. I see myself transitioning out of the lab at some point, but not yet. **I occasionally like to so experiments myself**. I could always go back into academia."

"The first barbecue I had in the garden of my house was a real highlight. And the first summer of Covid, when I went to Italy with friends and to see my family. It was nice to go to my home country with friends I'd made here."

Alessandro Cutilli

"I am going to take some time after the PhD ends to clear up my mind and recharge. I think am in a favorable position in which I can actually choose what I want to do, and I want to **step aside from academic research**. I have never been so aware of my freedom like I am right now.

I have no plans on moving out of the Netherlands at the moment."

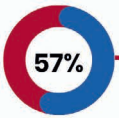
"I liked that my PhD project was not set in stone. It felt like it was unpredictable at times, but I had a certain degree of freedom to explore it in the directions I wanted. My PhD project had fantastic possibilities to answer biological questions, but I also had the full responsibility to make it successful and I felt alone in dealing with it. I am grateful for the chance to meet so many amazing friends along the way."

Zahra Shojaeijeshvaghani

"I want to go into the industry and work for a company. **I've never really envisioned working in academia for myself**. But first, I want to spend time with my family. Because of what is happening in Iran, we're all not in a very good mental place. It brings a lot of pressure, so first I'll need to organize my thoughts.

For now I'll stay here in the Netherlands. I have a baby boy and I'd like to raise him here. My husband also works here, and we want to stay and get our citizenship."

"This programme was a big opportunity for me that I'm grateful for, and moving here was super exciting, especially with such an international group of people. I learned a lot and gained many experiences."



of the students are open to **alternative jobs**

Vanessa Disela

"I am open to jobs in different fields, so I will look around and see what is possible.

I can imagine staying in the Netherlands, but it **depends on the opportunities**."

"I made close personal connections with the people in the programme and found so much support there. It's also been such a highlight to share a fascination about my project and the science around it with other people."

Laura Varela Pinzon

"I'm leaving academia. I like science and that it **feels like this big puzzle that you're trying to solve**. Generating knowledge is amazing. But I don't like the general system. I like project management and clinical research associate type of positions, or medical science liaison. But those are three completely different paths so **I'll need to figure out which suits me best**. I'm not excluding any options."

"I appreciated that the programme brought together a lot of people from outside at the same time. Nobody had any friends yet, so we became friends with each other."

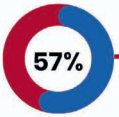
Aina Cervera i Barea

"I like science, but I might want to **get into more of a coordinating role**. In five years time, I see myself working four days a week, 9 to 5, so I can buy a house and **live my life without worries**. I know it won't be exactly like that, but at least I won't carry this big burden on my shoulders the way I feel it now.

I do miss home but the opportunities are not that well paid there. I already made the effort to move, so I'll stay for the next few years. Then **I'll see where life takes me**."

"I really grew as a person and I could have never done this without my friends. I've made friendships that will last a lifetime. I struggled a lot, but I'm happy with where I ended up and the progress I made. Overall, I would do it again."

Where do the students want to live after their PhD? While most leave their options open, they have expressed a preference:



of students would **stay in the Netherlands**

Laura Serini

"I am **thrilled to take the next step in my career** even thought I still have to decide whether I see myself more in academia or in a company. During my PhD, I have developed some interests in certain fields and I am looking forward to exploring these further.

I am enjoying my time here in the Netherlands and I am not planning to go back to Italy. I am **excited to see what the future will hold**."

"This was a great opportunity for me to purse a PhD in such a stimulating environment. The strength of the programme is to have the chance to bond with other internationals, who also just relocated to the Netherlands at the same time."

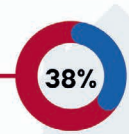
Su Ji Han

"I really have no idea yet. A post doc is still an option, but going to industries is as well. I will see how my last year goes and then I might also **attend some courses** to see what I'm good at or what I would like to do next.

Staying here would definitely be an option, but I am not restricting myself to the Netherlands only, it would mainly depended on the job opportunities."

"Looking back, I feel positive because of the people I've met. We were able to share our experiences and I think that's been something special. I feel like I've been lucky, and I've had good experiences here."

of students would **move back to their home country**



Sara De Palma

"I decided to put this decision off for another couple of months. **I do enjoy doing research**, but that doesn't necessarily mean I want to do a post doc. I don't think I'll continue in academia, because it's a lot. But it depends on what will come. **I still go back and forth on it**.

I want to live either here or back in my own country. I'll look for a position based on where I live."

"I've had ups and downs, but I've found a balance now. Conferences were a really cool experience, like this international one in the Netherlands. We stayed over with the whole group and it was really was really fun."

Nada Ristya Rahmani

"I'm expecting, I'm at seven months with my first baby. So I **don't want to make too many big decisions** until I know how I cope with that new life. I've joined a lot of career workshops, but made no decisions yet.

I will stay here with my husband for four to five more years, because he started a new job, and after that we'll go back to Indonesia."

"I'm very grateful. This was really a last opportunity for me to do a PhD. And me and the other students were very close in the beginning and we helped each other a lot. That all really helped in adjusting into the PhD life."

Jie Du

"I want to continue in academia, but in another area, **focusing on another disease**.

I am going to go back to China, to a city close to Hong Kong and start my post doc position."

"My highlight is this final stage of my PhD. I always wanted to go back to my family, but I got extension on extension, so I didn't go home for four years. I'm excited to finish up."

Lorenzo Costa

"I would like to do my **residency in orthopedics** first, and then after that I might also want to continue in research.

I would like to stay here. I was thinking of **doing a Dutch course**. But I might also go back to Italy, it depends on the opportunities."

"My first publication was an achievement for sure, and the first ethical approval. And I appreciate the bonding with the other RESCUE people who I will stay in contact with."

A final word from supersivors

"The RESCUE program has facilitated valuable connections between the PhD students which enabled them to **share knowledge and experiences**. This advantage became particularly important during the Covid19 pandemic. The **multidisciplinary research and training program** gave the students the opportunity to develop a broad range of skills and knowledge on many different topics. This reflects the field of regenerative medicine very well."

- Prof. dr. Roos Masereeuw

"For me and my group, it has been **rewarding to work with several international students**. Experiencing differences in culture and expectations was challenging at times, but identifying and overcoming these was a **great learning experience**. I highly enjoy working in such an international setting and the large cohort of RESCUE students was a true **boost to RM Utrecht**. It's a pity to see them leave now but all the bigger is the incentive to strive to realize another cohort in the near future."

- Dr. ir. Debby Gawlitta

"The RESCUE program brought us PhD students from completely different backgrounds and experiences, which **scientifically inspired the rest of our team** and the students they guided, and brought a multi-national and multi-cultural composition of the team and thereby years full of excitement and new insights. The corona-pandemic made it more difficult for them to experience the full-blown experience science can bring, with fruitful interactions and international traveling. Personally, **it brought me great joy to work with them**, get to know them personally and experience their habits and thoughts. I hope to be in contact with them in the future and further explore the regenerative approaches in our fields."

- Prof. dr. Joost Sluijter

"With Murillo, we gained an enthusiastic, talented and, above all, handy PhD student in the lab, with unprecedented perseverance. His Brazilian origin and general international experience **positively impacted the dynamics in the lab**. One time we were driving together to TU twente for work consultations and we drove under an ecoduct, causing disbelief. We even stopped to take photos to send to the home front in Brazil."

- Dr. Maarten Rookmaaker

"The RESCUE program enabled continued collaboration between my Equine Locomotion Research Group and the Research Group on Extracellular Vesicles headed by Marca Wauben. I appreciated the rules for recruitment in the cofund, which certainly have had a **positive effect on the diversity** among researchers. Laura Varela had a fascinating background with basic training in her native Colombia, a bachelor on genetics in Russia, and a master in Italy. While being hit hard by the pandemic that prevented her from travelling to see her family and reduced the number of secondments, Laura carried on very well. She is one of those PhD students that **give you energy and make you smile**, even if things are not going as expected or planned."

- Prof. dr. René van Weeren

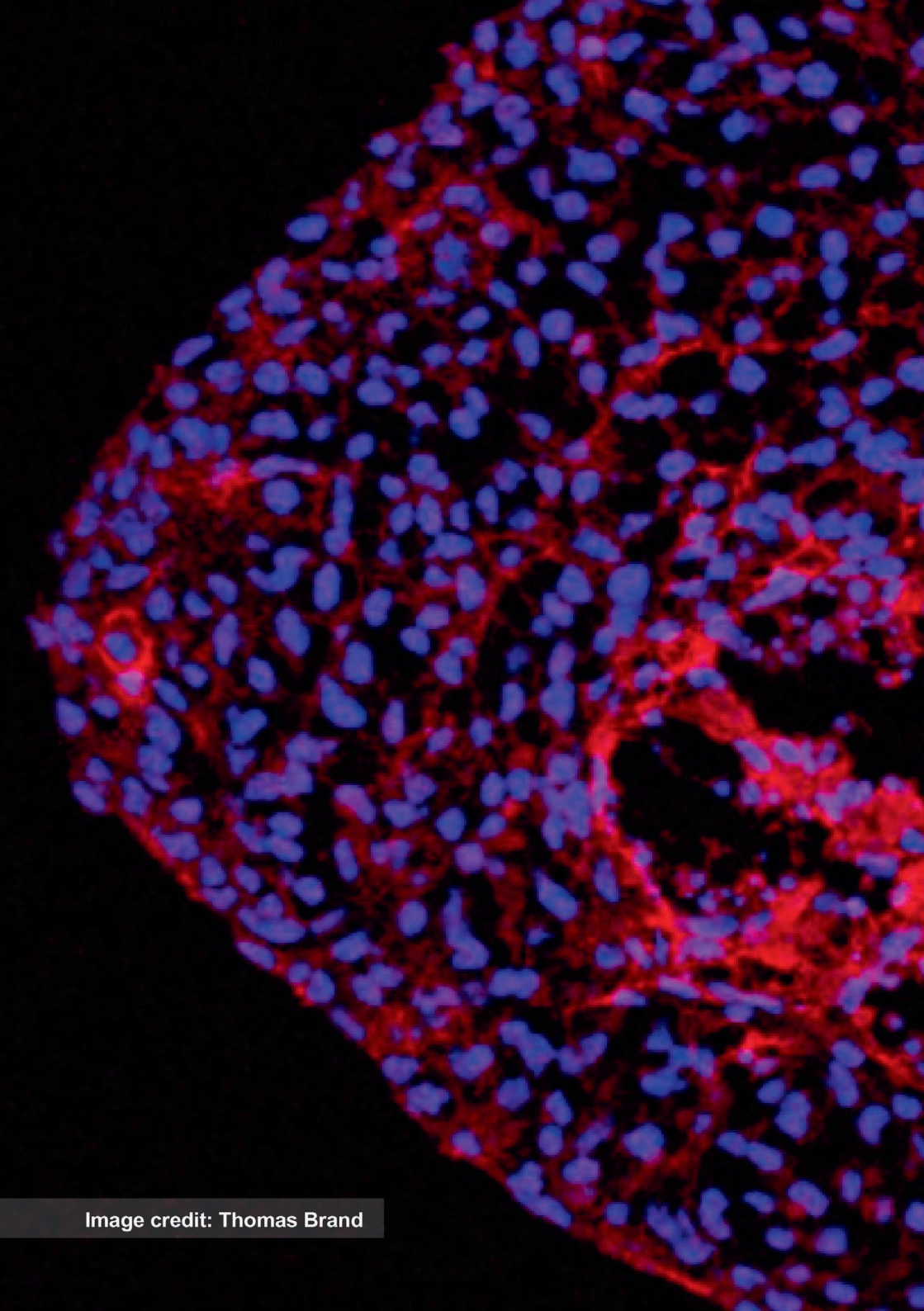
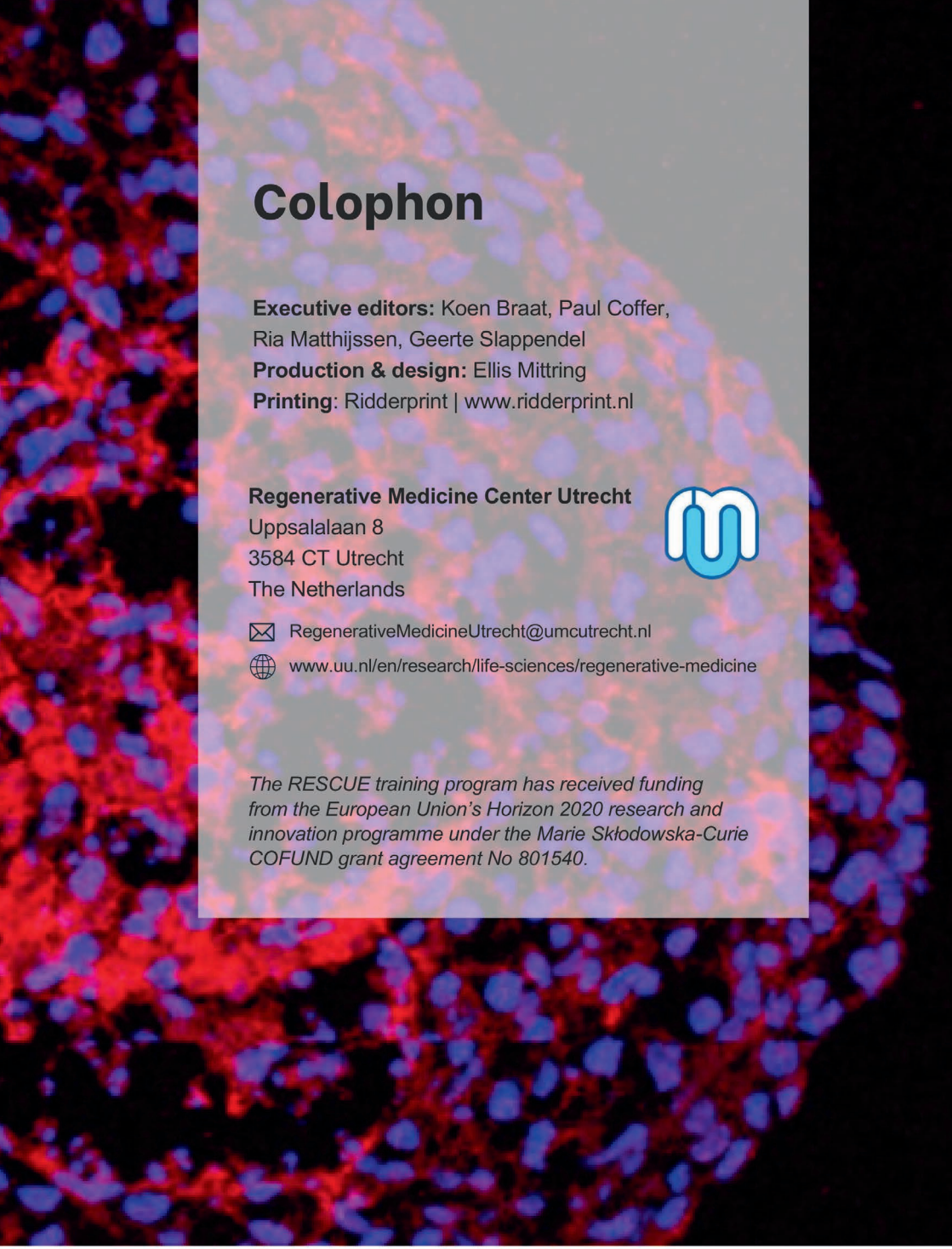


Image credit: Thomas Brand



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