The first four NUTRIM-NWO Graduate School laureates
"A PhD research project is like a painting"

In 2013 they were the first four young researchers to receive a prestigious NUTRIM-NWO Graduate School grant. They are hoping to complete their research projects, which they are completely organising themselves, in two years from now. How are they doing and what have they learned so far?

According to the NWO website, the goal of the NWO Graduate Programme is to strengthen the PhD system by offering highly talented young researchers a PhD position at an outstanding research school. They write their own research proposal, which has better chances if it is based on an interdisciplinary approach, and they seek out their PhD thesis supervisor themselves. This formula appealed to the four researchers who stopped by for the interview.

Birke Benedikter: "I really wanted to get a doctoral degree, but not just anywhere. I have specific interests and there weren't many existing projects that gelled with these. Two weeks before the decision on this scholarship was announced it turned out I had been accepted at another PhD location. But I said no to that, even though I had not yet received this scholarship. It was simply something I really wanted."
David van Dijk feels just the same: "I didn't want to do just any old PhD research and had been exploring my options for more than a year. I was very interested in cachexia and the theme fits this grant perfectly, because the problem doesn't play out just at the level of surgery. It's a metabolic issue and so it's a pretty obvious step for me to call on other expertise within NUTRIM. And now I'm more of my own boss, too: I myself chose what I wanted to research and how."
Jan Hansen adds: "I found it really important to create my own project, because it's amazingly motivating to research what you've come up with yourself. Of course, your supervisor helps you to steer your course, but you define your own direction. You don't have that position when you start a project where the professor already has a four-year plan ready for you."
Van Dijk: "If you've come up with it yourself, you know exactly why you've made certain choices and it's easier to take on the steering role."
Kiran Koelfat: "I come from the north of the Netherlands and actually I wanted to go back there after my master's, but then I got this chance to write a research proposal. This subject was very new here and the environment is outstanding for the work. NUTRIM is a leader in the field of metabolism, so I decided to keep going here. And this is a good place for translating things to the level of the patient. That's exactly what I wanted."

A big family

All four are working together successfully with various sections or departments within NUTRIM. Koelfat: "There's a great willingness to collaborate, and that's a nice thing about this big family."
Hansen: "There are many possibilities for studying the human metabolism, from mass spectrometry to the Metabolic Research Unit Maastricht (M-RUM), and of course the international network of professors." Benedikter: "My research and David's are now being linked up by someone from the latest group of laureates from the Graduate Programme." Hansen: "Because our projects are highly innovative and specific they're not so easy to connect. And precisely this innovation was an important criterion for this scholarship."
About once a year the researchers meet with the supervisory committee who selected them at the beginning of the process. Then they discuss the progress of the projects and with a supervisor. But the chances of this are fairly small, as they themselves recognise, because they have chosen their supervisors themselves.
"We knew who we would be working with," says Benedikter. In addition, this year they organised a mini-symposium at which they presented their research and they bump into each other in the corridors from time to time. Koelfat: "We're a group – it feels that way because we all started at the same time and in principle we'll be finishing together as

well. We support each other, although we don't see each other every week." This isn't so much at the level of content; it is more about moral support.
Koelfat chuckles: "Then, sighing, we say, 'We've only got two years left!'

Focus

And that brings the conversation to the lessons learned in the first two years.
Koelfat: "At a certain point I wanted to do far too many projects at the same time, but then my supervisor said – and rightly so – 'Focus'. You've only got four years and then you need to deliver a clear answer to a question."
Benedikter: "Your supervisor helps you keep your goals realistic."
Koelfat: "You're a bit like a young cook who opens a restaurant and has chefs from various restaurants looking over his shoulder."
Above all Benedikter has learned to deal with frustrations. "You often have a nice hypothesis and all the literature points in one direction; you feel sure that an experiment will deliver a certain result. But when you carry it out you get the opposite, or even worse, nothing happens at all, you become more realistic about what doing research really involves."
Hansen: "I see a PhD research project as being like a big painting. You paint and you think: 'This is going to be really nice, it'll be finished in four years and every detail fits perfectly.' And gradually you see: the bit at the top right doesn't fit completely yet and you'd do better to cut off the piece at the bottom left because it's not going to work out. It's a flexible work of art and you have to learn that it changes over time. It won't turn out the way you imagined at the start."
Benedikter: "If an experiment doesn't deliver what it's supposed to, then it's up to you to decide when to stop because otherwise it'll cost you a year."
Van Dijk: "What's very important for me is to achieve some success in the interim in order to keep going. Because my research is so broad I can always continue with something else if one area isn't going so well. Above all, I've learned to think scientifically. I had already done a fair amount of research, but I've become more critical and I now set up my research more thoroughly. At congresses I'm much more critical about other research. I now see basic mistakes in other people's results that I didn't notice before."
Hansen: "You start to feel a sense of responsibility. All the data you send out into the world will be examined by everyone and basically they assume that what you have published is correct. So you also become more critical of your own work."

Looking ahead

After another two years, the four years will be over.
Van Dijk recently had a long talk with his supervisor in which they discussed what has been achieved and what should be realistic to complete before the summer of 2017. "Then the scholarship will really be over, so it's important to finish then."
Benedikter: "It's hard to look ahead because you never know how things will go. In the first six months I didn't look ahead at all, and then the next six months went faster than expected. Sometimes you spend months on something you thought you could complete within three weeks. But I assume that I'll get it finished on time."
Koelfat: "A PhD is a process with ups and downs, and you spend most of the last year writing your papers. At the moment I'm still mostly busy collecting lots of samples."
Hansen: "After nine months I had to troubleshoot and remove a large part of my dataset, because unfortunately it didn't produce anything. Oh well, that's part of the work," he laughs nonchalantly. Asked about this, he says: "I've got through the denial phase and now I'm in the acceptance phase. It would have been a nice cherry on the cake, but the study still stands."

Permanent position

For two of the four the future is still not set in stone.
Hansen: "I would like to continue doing research, and preferably in this field. I find the subject really interesting and I've already invested so much time in it that I've become

part of the research community. But I don't know whether this would be at a university or at a company."
Benedikter: "I enjoy doing research and would like to continue for another ten years. I also really like teaching, going to congresses and brainstorming with other scientists. The nice thing about this work is that you are constantly being encouraged to develop your abilities. But the research world is very uncertain, too. I would like to get a permanent position fairly soon, instead of having to move every two years - possibly with a young family - to another post-doc job."
The ultimate role model for the two soon-to-be surgeons is Steven Olde Damink, who also combines work as a surgeon with a professorship, including a large laboratory and teaching tasks.
Van Dijk: "I think that as a doctor you can easily bring research to the clinic doctors time for scientific research, so you don't have to do it all in your own time."
Koelfat: "Although Steven also devotes his day off to science."
Van Dijk: "Surgery is becoming ever more specialised: you need to do a minimum number of surgical procedures per year in order to be allowed to carry out a certain procedure, so if you decide to do more science, you have to be careful not to lose too much clinic time."
Koelfat: "Olde Damink is a role model because he seems to have found the balance between many different activities."

• David van Dijk (1987) studied medicine and then worked for a year and a half as a resident in the intensive care unit and the surgery department at Atrium MC in Heerlen. In 2013 he was hired at the Surgery Department of the MUMC+ to write a research proposal. The NWO Graduate Programme appealed to him because it offers participants the chance (and encourages them) to work on an interdisciplinary basis. "I work with more sections and departments at NUTRIM than I can count. I consciously chose to do broad research because I want to learn as much as possible in these four years."
Van Dijk is researching the extreme loss of weight and muscle (cachexia) suffered by cancer patients, especially those with pancreatic cancer. He is investigating various points of departure that could explain this extreme cachexia: protein metabolism, bacteria in the intestine, malabsorption and the destruction of fat and muscle cells by tumour cells.

• Birke Benedikter (1989) works in the Medical Microbiology and Respiratory Medicine Departments where she researches extracellular vesicles in Chronic Obstructive Pulmonary Disease (COPD); vesicles are small membrane bubbles or blisters secreted by cells which, thanks to their content (proteins, RNA, lipids) can influence the behaviour of other cells. "It has been established that these vesicles contribute to processes of inflammation in the lung such as asthma and sarcoidosis, but little is known so far about their role in COPD." Benedikter hopes to change this situation, for instance by using mass spectrometry. During her graduation internship in the Maastricht research master's in Biomedical Sciences she already worked on a small research proposal while at the Department of Medical Microbiology. "I don't like being told what I should research; I want to determine that myself. And that's something that immediately appealed to me about this scholarship."

• Jan Hansen (1986) also did the research master's in Biomedical Sciences in Maastricht, after having attended the Excellence Bachelor's Programme in Molecular Medicine in Germany and having worked as an analyst for a year and a half. During his graduation internship with Prof. Patrick Schrauwen he studied metabolic disruptions in diabetes sufferers. Now, as part of the Human Biology Department, he is investigating whether these disruptions are related to the biological clock and whether this interaction can cause obesity and type 2 diabetes. "Over the last hundred years this clock has had to deal with the changes in lifestyle, such as 24/7 lighting, more food and less exercise. If you force mice to eat during the inactive phase of the day, for instance, then they get fatter than the mice who receive the same calories in the active phase.

I’m researching how the cell can use this clock to switch metabolic processes on and off as required. And which genes in that process can be related to target genes which we know are disrupted in obesity and type 2 diabetes.” He is working at both the cellular level and with human studies.

• Kiran Koelfat (1985) completed the four-year Doctor-Clinical Investigator (AKO) master’s
in Maastricht. “I always wanted to be a doctor, but it was only through research activities during my bachelor’s that I also became interested in research.” The combination of clinical work and science is also reflected in his research subject. He is investigating the consequences of disrupted bile salt signalling for intestinal and liver function in patients with a perturbed enterohepatic cycle (the circulation of, among other things, bile salts between the intestine and the liver). Bile salts carry out important signalling function by activating nuclear and membrane-bound bile salt-sensing receptors present in both the small intestine and the liver. An interruption of this cycle causes intestinal and liver dysfunction, especially in patients with intestinal failure (short bowel and enterocutaneous fistulas). During his master’s internship he discovered in a surgical animal model of an interrupted enterohepatic cycle that the activation of a bile salt receptor prevents liver damage and reduces the loss of intestinal fluid. In his PhD research project he hopes to translate this knowledge to the level of the patient by testing the concept in a relevant patient population