Stem cell among scientists

Biologist or physicist? Superstar or shy colleague? Researcher or director? Is he Dutch or American, data geek or rock musician? **Alexander van Oudenaarden** (47), winner of the 2017 Spinoza Prize, is not easily pigeonholed. Who is he really, and what could account for his success? His fellow scientists offer a few suggestions.

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The scene could have been taken straight from a movie script. An unexpected late night call. An unfamiliar voice extending congratulations out of the blue. A curious spouse straining to catch a word or two from the couch, followed by a grin that slowly lights up the face of our protagonist. The only thing missing would be a shouted 'cut!' from a director.

That was a few months ago. 'The toughest part was keeping mum', says Anna van Oudenaarden, Alexanders Russian-born wife and colleague. 'For weeks, we couldn't tell anyone about that phone call.'

When the news finally broke, it raced through every last corridor and laboratory at Utrecht's Hubrecht Institute, instantly reaching the ears of its two hundred-odd biologists as they grappled with the mysteries of stem cells. Their director Alexander van Oudenaarden, the man whose CV was already too hefty to staple together, had been awarded the single most prestigious science grant in The Netherlands; the NWO Spinoza Prize.

His predecessor had predicted as much at Van Oudenaarden's appointment in 2012: 'We've landed a superstar.'

Superstar or shy colleague?

Say, you've been assured your entire life by those around you that you are extremely smart. You get a degree, a PhD, do research and, to your delight, make it to professorship. But then, suddenly another researcher comes to work at the lab. Someone who, never blinking an eye, comes up with solutions to the complex conundrums you have tried to tackle for ages. A person constantly showered with praise, prizes and promotions. If a journalist ever finds their way to your desk – all you're asked is questions about this 'superstar'. Surely, some envy would only be natural?

Not if said superstar is Alexander van Oudenaarden. 'I recall the first time I saw him', says Jacco van Rheenen, professor of intravital microscopy at Utrecht University and UMC Utrecht, as well as group leader at the Hubrecht Institute. 'There he was, attentively poring over his microscope. That must have been around 2008, when he took a sabbatical at the Hubrecht Institute. I got to know him as an amicable, enthusiastic scientist. I didn't have a clue then that he already was quite the big shot in America, leading a top team at MIT. He never bragged about those things. He is outstanding, but a little shy as well. That's why no one begrudges him anything.'

It was already clear even back then, that Van Oudenaarden takes a different approach to science than from the rest of the Institute. 'We're all biologists here', says Rik Korswagen, professor of molecular developmental genetics. 'At MIT, Van Oudenaarden was professor of biology as well as professor of physics. He even holds a PhD on solid state physics – you really can't get much closer to the ultimate in physics. That gives him a unique perspective in his work.'

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Biologist or physicist?

In the world of science, where experts from one field wouldn't understand the first thing about studies in another field, Van Oudenaarden's polymathy is crucial, says Utrecht University professor of developmental biology Sander van den Heuvel. 'As elsewhere, enormous amounts of data are generated within the field of biology today. Many biologists are unsure how to handle that. Maths, to them, is a foreign land.' Where many biologists falter, Van Oudenaarden goes the distance. Using techniques of his own design he plunges into the individual cell, hoping to piece together exactly what goes on inside. Why is it that a stem cell becomes a spermatozoid, not a hair cell? 'His razor-sharp insights were of great help to us all', Korswagen recalls. 'Yet I never thought we would see him return here after his sabbatical. Why would he? Didn't he have a dream job in America?'

Anna van Oudenaarden has the answer. 'That sabbatical was an excuse. He wanted his children to grow up in the Netherlands. It was for that reason he decided to try working in the Netherlands – something he had never done.' It became official in 2012: the superstar would return to the Hubrecht Institute, as director.

'That did raise a few murmurs', Van Rheenen remembers. 'Great guy, and a fine scientist; but did he have the experience and authority for the position?'

Researcher or director?

Van Oudenaarden was not without doubts himself. After all, he was a scientist through and through. A man driven by the urge to discover why things are the way they are. Though not religious, given the eternal life he would certainly spend the first millennium on the celestial plane – well, probably playing guitar. 'But in second place, he'd definitely choose performing hard data-analyses. He sincerely enjoys it', his wife Anna knows.

As director, Van Oudenaarden was dealt a different hand of tasks. Meetings, logistical problem-solving, firing employees, acquiring funds, appeasing politicians and journalists alike. 'That last area was a forte of his predecessors Ronald Plasterk and Hans Clevers. Knowing that was part of his trepidation. Multi-talented as her husband might be, he never was the type to take the stage and showcase a set of opinions to his audience.

Still, he did not shy away from the challenges of the director's office. A decade at MIT had turned him into enough of an American to embrace their typical can-do attitude.

Dutchman or American?

He met his wife in the United States, his three kids were born there and with his rock band Asymptonic Freedom Van Oudenaarden let it all hang loose on stage. 'And yet, Alexander hasn't been completely Americanised', according to Van den Heuvel. 'He doesn't expect his co-workers to be at work eleven hours a day. He himself isn't either. We live in the same town, and I often see him taking his kids to school, by bike.'

'He's not trying to turn the Hubrecht Institute into an MIT clone', says Van Rheenen. 'The main difference? At MIT, research groups are forever trying to one-up one another. Everyone is in competition. The Hubrecht Institute is also performance-oriented, but Van Oudenaarden likes his institute with its specific Dutch flavour.

For example, as soon as he was appointed the new director opened every door to his own research group. He started talks with scientists from other teams and came up with new ways in which they could assist one another. Co-operation became the magic word.

'There are so many examples', Van Rheenen recounts. 'Recently, my group used highly sophisticated cameras to record how stem cells in mice adapt into mammary gland cells. Subsequently, Van Oudenaarden dived into individual cells, using his technology to collect more precise data on RNA expression. Both methods are unique, yielding insights on the way cells are supposed to function. That, in turn, allows us to better determine which kind of glitch could theoretically lead to cancer', explains Van Rheenen.

Since then, cooperation has become ingrained in the Institute's culture; collaborations are even forged across the coffee table between PhD candidates. 'Everyone realises that elbowing one's way to the front is not necessarily appreciated.' Van Rheenen concludes.

Colleagues are unanimous in their verdict: as director, Van Oudenaarden has continued to excel. Korswagen: 'Filling Clevers' shoes was no easy task, but he succeeded, on his own terms.'

Single-cell or multicellular?

In the archipelago of science, full of isolated isles of research, Van Oudenaarden has emerged as its ideal physicist-biologist, researching-directing, rocking, geeky, Dutch-American competitive team-oriented builder of bridges. In the evolution of life, the transition from single-cell to multicellular life was a crucial stage. Suddenly individual cells were no longer fated to fight amongst themselves, but could strive towards higher goals, each through their own specialisation.

That is exactly how Van Oudenaarden envisions the Hubrecht Institute. Individual research cells should not compete, but rather strengthen each other like cells of a multicellular life form, working towards a transcendent objective: to accrue knowledge. As Spinoza wrote: the aim should be to be to find that which is unlimited and eternal, and can be owned by all. ■

CV

Alexander van Oudenaarden
Born 1970 in Zuidland (South Holland, the Netherlands)

- **1998** PhD applied physics (cum laude) at TU Delft
- **1998** Postdoc at Stanford University
- **2000** Transfer to MIT, Boston
- **2004** Associate professor, MIT
- **2008** Professor of Physics, MIT
- **2009** Professor of Biology, MIT
- **2012** Research director at Hubrecht Institute (KNAW)
- **2012** NWO VICI grant
- **2013** Professor of Quantitative Biology of Gene Regulation, UU/UMC Utrecht
- **2017** NWO Spinoza Prize

Second to playing the guitar, Van Oudenaarden's favourite activity is analysing data.