


PEOPLE & IDEAS

Sarah-Maria Fendt: Driving scientific discovery through collaboration

Stephanie Houston 

Sarah-Maria Fendt is a principal investigator at the Flemish Institute for Biotechnology (VIB) in Belgium, and her laboratory focuses on cellular metabolism and metabolic regulation. Recent work from Sarah’s laboratory has shown that pyruvate available in the metastatic niche enables cancer cells to shape their environment and promote metastatic outgrowth. We contacted Sarah to find out more about her journey in science so far.

Where did you grow up?

I grew up in a very small village in Bavaria in the south of Germany, a 45-min car ride away from any bigger city. It was a fantastic place to grow up as a kid because I was able to spend my childhood with friends playing in the meadows and woods around the village. When I became a teenager, however, I was very happy that, by turning 15, I received my motor scooter driver’s license. This allowed me to visit school friends living in the next valley without the need of always relying on the bus or my parents to drive me. It was a fun, happy, and protected youth.

When did your interest in science begin? What was your first experience of science?

I became interested in science during my last years of high school. I chose mathematics and chemistry as major subjects for my high school degree (Abitur), and I just loved it.

Where and with whom have you studied (undergraduate, graduate, postdoc)?

I would say my studies can be best summarized by a quote from Douglas Adams: “I may not have gone where I intended to go, but I think I have ended up where I needed to be.” In this respect, I started after high school to study chemical engineering at the Technical University in Munich, but I realized during my freshman year that I did not want to design, engineer, and understand chemical processes, but that I wanted to understand life and disease. Therefore, I switched my subjects and enrolled in biochemistry as a major. Regardless of this

switch, I did stay close to engineering and decided to do my master’s thesis at the Danish Technical University in Lyngby in the Department of Micro- and Nanotechnology, developing a microreactor allowing rapid sampling of bacteria cultures for consecutive metabolomics analysis.

With my PhD at the Department of Molecular Systems Biology at ETH Zurich in Switzerland, I added, on top of biochemistry, a deeper understanding of the global regulatory principles of metabolism by studying the transcriptional regulation of metabolic fluxes in yeast in the laboratory of Uwe Sauer, who is at the forefront of metabolomics and systems biology research. My PhD project allowed me to foster my love for quantitative data, overarching mechanisms, and metabolism. Uwe always provided his students and postdocs with a lot of freedom in leading their projects. And so, I chose to not only focus on my main research project, but also to engage in a close collaboration with one of my colleagues. This was an incredible experience because it fostered my outside-the-box thinking, and I realized that collaborations can be truly synergistic. A result of this fruitful collaboration was a publication that turned out to become my best-cited PhD work (Fendt et al., 2010).

After my PhD, I decided that it was time to combine my passion for metabolism and systems biology with my interest in medical biology and especially cancer research. To do so, I started a postdoc at Harvard Medical School in Boston in the Department of Systems Biology. My ambition was to do cancer metabolism research in the laboratory of Galit Lahav, who is a leader in single cell



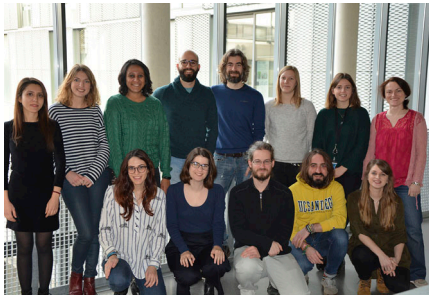
Sarah-Maria Fendt. ©VIB, IneDehandschutter.

research and regulation of cell fate by p53. Unfortunately, the project failed, and after seven months in Galit’s laboratory I was confronted with the choice of either giving up on metabolism or searching for a new laboratory where I could follow my goal of investigating cancer metabolism. I chose the latter and switched to the laboratory of Greg Stephanopoulos at the Massachusetts Institute of Technology (MIT). In some way, this brought me back to my roots, because Greg is located in the Department of Chemical Engineering and is renowned for his groundbreaking research in metabolic engineering. In addition to biotechnology-oriented metabolic engineering, he also

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The Fendt lab, December 2018.

had a great interest in cancer metabolism, and so I joined his laboratory in which many of my current colleagues in the field of metabolism had trained. Not that long before I started in Greg's laboratory, Matt Vander Heiden had joined the faculty of MIT, which turned out to be relevant for my postdoc research. Matt is a highly recognized pioneer of cancer metabolism research, and since Greg provided me with all support and freedom to develop my own research line, I established a close collaboration with Matt's laboratory. Therefore, I had the best of two worlds: on the one hand I had the strong expertise and support in data modeling, mass spectrometry analysis, and metabolic flux regulation from Greg's laboratory, and on the other hand I had the cancer, disease metabolism, and *in vivo* expertise from Matt's laboratory. Building on this amazing opportunity allowed me to integrate the idea of metabolite concentrations regulating metabolic activities into the context of cancer (Fendt et al., 2013). This "best of two worlds" situation fostered my scientific growth, which allowed me to catch up time by finishing my "second" postdoc within two years. In summary, my way from undergraduate studies to successfully finalizing my postdoc was everything but straight; yet each of these steps was important for my personal and scientific development, and I wouldn't want to miss out on any of these steps or experiences.

What interested you about your current area of study?

For the past six years, I have had my own laboratory at the VIB-KU Leuven Center for Cancer Biology in Belgium. We are interested in the role of metabolism in metastasis formation. My interest in this topic is two-fold. On the one hand, metastasis formation

is the leading cause of death in cancer patients, and currently we have no effective treatment to inhibit the spread of cancer cells from the primary tumor to distant organs. Thus, being able to identify a treatment that prevents or at least reduces the chance for metastasis formation will have a dramatic impact on patient survival. On the other hand, metastasizing cancer cells need to be highly plastic. To successfully transition through the metastatic cascade, cancer cells change their cellular phenotype. For example, while proliferation is an important phenotype in a growing primary tumor and an established metastasis, proliferation is less important during metastasis formation. This is the case because cancer cells need to gain the motility to invade the surrounding tissue, they need to survive in the circulation, and they need to seed and colonize in distant organs. Thus, the cancer cell phenotype is highly plastic. Moreover, when cancer cells reach a distant organ, they do not necessarily have access to the same nutrients as in the primary tumor, and since metabolism connects the available nutrients to the cellular phenotype, I strongly believe that targeting metabolism will be an important way to tackle metastasis formation.

What are you currently working on? What is up next for you?

At this moment, we mainly focus on understanding the metastatic spread of breast cancer cells to the lung (Christen et al., 2016; Elia et al., 2017, 2019). In the near future, we will also research other metastatic sites and cancer cell origins, as well as better understand the interaction of metastasizing cancer cells with stromal cells.

What kind of approach do you bring to your work?

I deeply care and love my work, and I always try to light the same fire in my team members by supporting them by all possible means and by challenging them to take the lead on their research.

What did you learn during your PhD and postdoc that helped prepare you for being a group leader? What were you unprepared for?

For me, the four most important things were: (1) Have a hypothesis or goal and follow it with creativity and endurance

along the path the data lay out for you; (2) Collaborate and surround yourself with excellent peers who challenge you to grow and leave your comfort zone; (3) Combine your expertise with something new in order to evolve and make a unique contribution; (4) Take feedback seriously and as an opportunity to improve.

It sounds obvious, but hiring, mentoring, teaching, planning, and securing funding as a principal investigator is very different compared with my experience in these topics as a PhD student and postdoc.

What has been the biggest challenge in your career so far?

In the end, every challenge is an opportunity, and so far, from all of the challenges I experienced, I have learned something.

What is the best advice you have been given?

Trust your gut feeling.

What hobbies do you have?

I love traveling, hiking, and food. I go running on a regular basis and I sing in a choir.

Any tips for a successful research career?

Seek collaborations; such scientific interactions, in my experience, often result in truly interesting findings (Vriens et al., 2019). Watch out for the unexpected, listen to feedback, and encourage independent and outside-the-box thinking. Always have a hypothesis, but constantly adapt the hypothesis to the data. Surround yourself with excellent peers who challenge you and support you in evolving beyond your comfort zone. Do not be afraid of making tough decisions. Look for potential and diversity in people, in addition to expertise. Hire people who truly care about their work and research.

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