THE AUTHOR FILE

Marlon Stoeckius

Combining approaches from "different worlds" to learn more from a single cell.

"I was the first, basically, guinea pig of this program," says Marlon Stoeckius, research scientist at the New York Genome Center, about what has become a transatlantic PhD exchange program. While working on his PhD degree at Humboldt University in Berlin, he was a member of Nikolaus Rajewsky's lab at Max Delbrück Center for Molecular Medicine in Berlin and did stints with developmental biologist Fabio Piano at New York University (NYU). As the first high-throughput sequencers arrived in Berlin, Stoeckius began melding technology with his *Caenorhabditis elegans* research. He hacked a flow cytometer to sort thousands of one-cell worm embryos and explored how to combine transcriptomic and proteomic measurements, for example, for measuring proteomic differences between oocytes and one-cell embryos.

V. Barcan

Marlon Stoeckius

After finishing his PhD, Stoeckius became a fellow in Rajewsky's newly founded systems biology institute. Eager to apply his research skills to a vertebrate, he joined Antonio Giraldez's Yale University lab as a postdoctoral fellow, working on zebrafish development. He considered faculty posts in his native Germany, but technology development had a stronger appeal. He wanted to pursue questions such as, "How can I answer a certain question with a certain technology? How can I 'mod' the technology?" In 2015, he joined the new Technology Innovation Lab at the New York Genome Center, where he and his colleagues have developed a high-throughput way to simultaneously measure single cells inside and out.

The team's CITE-seq approach, for cellular indexing of transcriptomes and epitopes by sequencing, uses DNA oligonucleotides conjugated to antibodies and droplet-based sequencing library preparation. CITE-seq delivers multiple layers of information about single cells in ways previously not possible, says Stoeckius. It can profile cell surface proteins and transcriptomes from a few thousand single cells at a time, with the potential to profile hundreds of thousands of cells.

The researchers tested CITE-seq with two single-cell library prep systems: Drop-seq, which scientists can build in their own labs, and the 10X Genomics commercial instrument. Stoeckius says CITE-seq works with any method that encapsulates single cells. The scientists have worked with 17 antibodies; now they are starting a 70-antibody panel, and want to go higher. The New York Genome Center has patented CITE-seq. Labs have long used flow cytometry for immunophenotyping. They leverage the way antibodies with attached fluorophores latch on to surface proteins to mark, for example, which cellular pathways might be turned on. But flow cytometry does not typically profile RNA. Labs performing single-cell RNA sequencing know their cells' RNA but not the effector molecules decorating the cells' surface. In many ways, these are "almost like two different worlds," says Stoeckius. CITE-seq connects these worlds and can shed light on many aspects of post-transcriptional regulation of RNA and proteins in single cells. It might help Stoeckius decipher mysteries such as the regulatory flurry of activity in a single one-cell embryo.

Dominic Grün, group leader at the Max Planck Institute of Immunobiology and Epigenetics in Freiburg, worked with Stoeckius in Rajewsky's lab and calls him the kind of student any principal investigator would wish for. He enjoyed research and loved to explore new technologies, "and you could feel this spark of inspiration," says Grün. Stoeckius looked at subjects from many angles, creatively, with a hands-on attitude, and performed challenging experiments to prove his point. "I remember him sitting at the microscope when I arrived in the morning and still being busy pipetting when I left in the evening," he says. "With his unconventional open-minded way of thinking, he certainly influenced my way of doing science."

"How can I 'mod' the technology?"

Stoeckius is happy at the New York Genome Center because he has always sought out labs with a collaborative and pioneering spirit—and good espresso, which helps him discuss ideas, write, find inspiration and recharge. "What I realize now, what I really think is very exciting is to be in an environment that's really new," he says. For scientists starting out, he recommends they follow ideas that speak to them. "Lab work can be really depressing and if you do something in the lab that you don't like, you should rather work on something your heart is really burning for," he says. In New York City, he enjoys many of his favorite pastimes from Berlin, a city renowned for its electronic music scene. He has made some good discoveries in Brooklyn's warehouse-basement clubs and regularly takes in live jazz music, too. He bikes, runs and explores New York's cultural offerings. "Every weekend essentially looks different," he says.

Vivien Marx

Stoeckius, M. *et al.* Simultaneous epitope and transcriptome measurement in single cells. *Nat. Methods* **14**, 865–868 (2017).