

## CORNELL CHRONICLE

### Elegant trick improves single-cell RNA sequencing

By Tom Fleischman | December 19, 2018

Droplet microfluidics has revolutionized single-cell RNA sequencing, offering a low-cost, high-throughput method for single-cell genomics. However, this method has been limited in its ability to capture complete RNA transcription information.

Researchers at Cornell – led by Iwijn De Vlaminck (<https://www.bme.cornell.edu/faculty-directory/iwijn-de-vlaminck>), assistant professor in the Meinig School of Biomedical Engineering – have come up with an elegant, low-cost method that solves that problem. And not only does it push single-cell genomics forward, it may allow for new avenues for studies of infection and immune biology.

“**Simultaneous Multiplexed Amplicon Sequencing and Transcriptome Profiling in Single Cells** (<https://www.nature.com/articles/s41592-018-0259-9>)” was published Dec. 17 in *Nature Methods*. Postdoctoral researcher Mridusmita Saikia and doctoral student Philip Burnham, both of the De Vlaminck lab, are lead authors.

Also contributing were Charles Danko, assistant professor at the Baker Institute for Animal Health in the College of Veterinary Medicine, and John Parker, associate professor of virology in the Baker Institute.

In 2015, researchers from Harvard University and the Massachusetts Institute of Technology introduced Drop-seq, a method to simultaneously and efficiently characterize the identities of thousands of cells, using nanoliter-scale droplets and attaching a unique identifier to each cell’s RNA.

“Those technologies are very popular because they’ve lowered the cost of these types of analyses and sort of democratized them, made them very cheap and easy to do for many labs,” De Vlaminck said.

The drawback, however, is that they can only identify a certain type of messenger RNA (mRNA) molecule, which limits the potential scope of analyses. Messenger RNA carries the genetic information copied from DNA in the process of translation.

De Vlaminck and his collaborators have come up with a simple, inexpensive twist to the existing Drop-seq protocol, and call their new method DART-seq (droplet-assisted RNA targeting by single-cell sequencing).

In Drop-seq, individual cells are encapsulated with labeled microparticles that initiate reverse transcription of cellular mRNA. The De Vlaminck group devised an effective method to enzymatically customize the beads prior to performing conventional Drop-seq analysis, which allows for the recovery and analysis of a greater variety of molecules than are available through Drop-seq sequencing.

In addition, this technology can identify virus-infected cells, and quantify viral and host gene expression, thus enabling examination of the host response to infection at single-cell level.

“A single virus species can be very diverse, and that diversity permits them to do extraordinary things,” Burnham said. “So if you can zoom down to the single-cell level, you can actually see how minor changes in the virus cause a potentially huge change in how the cell reacts to that small mutation.”

Saikia, who has a dual appointment with the veterinary college, thinks DART-seq will also help inform new approaches to cancer therapy.

“Cancer cells are a very heterogeneous population,” she said, “and when you don’t look at them at the single-cell level, you often miss important information. So our technology also allows that.”

Other contributors included doctoral student Michael Wang and undergraduates Sara Keshavjee ’19 and Michael Heyang ’19 at the De Vlaminck Lab, and postdoctoral researcher Pablo Moral-Lopez and research technician Meleana Hinchman of the Parker Lab.

Sequencing experimentation for this paper was performed at the [Cornell](#) Biotechnology Resource Center.

The work was supported by grants from the National Institutes of Health and the National Science Foundation Graduate Research Fellowship Program.

#### MEDIA CONTACT

**Jeff Tyson**

[jeff.tyson@cornell.edu](mailto:jeff.tyson@cornell.edu) (<mailto:jeff.tyson@cornell.edu>)

↳ (607) 793-5769 (<tel:607297935769>)

#### YOU MIGHT ALSO LIKE



Cell-free DNA may be key to monitoring urinary tract infections

(</stories/2018/08/cell-free-dna-may-be-key-monitoring-urinary-tract-infections>)



Four on faculty receive NIH high-risk, high-reward awards

(</stories/2017/10/four-faculty-receive-nih-high-risk-high-reward-awards>)